VOL. CL, No. 2 AUGUST, 1915 No. 521

THE AMERICAN JOURNAL OF THE MEDICAL SCIENCES

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THE

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AUGUST, 1915

ORIGINAL ARTICLES

RAYNAUD'S SYNDROME: RAYNAUD'S DISEASE.

By Oliver T. Osborne, M.A., M.D.,

PROFESSOR OF THERAPEUTICS, YALE UNIVERSITY, NEW HAVEN, CONNECTICUT.

Maurice Raynaud was a French physician, and lived from 1834 to 1881. The disease which bears his name was first described by Sir Benjamin Brodie in 1837, but was not recognized as a disease until it was described by Maurice Raynaud in 1862, under the name of "symmetrical gangrene of the extremities." The condition was not known as "Raynaud's disease" until his second article, which more fully discussed it, in 1874.

The disease or condition was first termed "local asphyxia and syncope;" it has also been termed "symmetrical gangrene." The latter name is a misnomer, as the local manifestations are as frequently unilateral as symmetrical. Raynaud's belief that the local symptoms were caused by a spasm of the capillary vessels, which shut off the circulation more or less permanently from a part, is correct. Pathological investigations have shown there is no primary disease of the walls of the vessels.

The syndrome may be defined as a condition with such vascular disturbance as to cause a more or less complete anemia or a prolonged passive hyperemia of various parts of the body, internal as well as external. No definite cause for this idiosyncrasy or peculiar instability of the bloodvessels has been discovered. There may be a local spasm of the arterioles or venules, or of both. If the arterioles are contracted the cyanotic type of congestion occurs, preceded by an anemia; if the venules are alone contracted, a hot, congested form, slightly simulating erythromelalgia, may occur.

The associated symptoms due to this bloodvessel spasm are more or less pain, coldness or iciness to the feel, numbness, later impaired function, and trophic disturbances, as shown by eczemas, small blisters, bullæ, ulcerations, suppurations or even gangrene, sloughing, and loss of the part affected. The joints of the fingers may become sore and inflamed, and ulcers often occur near the nails with deep suppuration in and around the nails. The parts affected temporarily or interchangeably during a certain period may be symmetrical, but are not necessarily so. The spasm of the bloodvessels may last minutes, hours, or days.

The simplest form of this disease is represented by cold hands or feet, or by a finger or a toe becoming stone-cold, termed "dead finger" or "dead toe." The obstruction to the circulation may attack several fingers or the whole hand, the whole foot, the nose, an ear, or there may be serious bloodvessel disturbances of the internal organs of the body. The first local symptom is coldness and anemia, with or without pain, followed perhaps by an asphyxia or a darkening of the part; and later a hyperemia may occur, with flushing and increased local circulation. In the very mild forms the local condition is similar to that of a frost-bite, with burning, itching, and later heat succeeding the coldness and anemia of the part. This symptom complex may recur and continue to recur in the same fingers or toes. There are often pigmentations, mottling, and brown spots on the skin on various parts of the body.

In a few instances recognized, and in many instances unrecognized, this syndrome is the cause of various abdominal disturbances and of disturbances of the nervous system. There may be a spasm of the retinal vessels and temporary loss of vision. There may be loss of hearing and disturbances of the senses of taste and smell from contraction of the bloodvessels. There may be loss of speech, dizziness, paralysis, psychic disturbances, epilepsy, and cataleptic symptoms from these bloodvessel disturbances. Severe, intense headaches may occur, with burning sensations of the face and head and hot flashes. The menopause symptoms show in a mild form this vasomotor instability. There may be such disturbance of the bloodvessels in the head as to give a feeling of constriction. This is the kind of headache that is complained of by some individuals.

It is possible that some forms of epilepsy without any assignable lesion may be due to this peculiar disease. At least it is interesting to note that such cases of epilepsy as have an aura may sometimes have an attack aborted by the inhalation of such a vasodilator as amyl nitrite.

Temporary loss of muscle power and sensations and momentary paralyses may be due to spasms of the bloodvessels in certain areas of the brain. Temporary or recurrent albuminuria, and even hematuria, may be caused by sudden spasms and later congestions of the

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renal vessels. In other words, this bloodvessel spasm is the cause of many apparently serious nervous disturbances and of many abdominal disturbances that have led to operation, and yet nothing pathological has been found. Such contractions of the bloodvessels in the abdomen generally cause pain, and may cause distention, vomiting, and symptoms simulating all kinds of colics.

Edema of the face or of one or more extremities may occur, and may suggest angioneurotic edema. There may be symmetrical swellings of the extremities in both angioneurotic edema and in Raynaud's disease. There may be paroxysms simulating malarial fever, with chills and subsequent high temperature.

The disease is not a pathological entity. It is caused, the writer believes, by disturbances of several of the internal secreting glands, especially of the thyroid and suprarenals, and also perhaps of the ovaries. The disease is frequently associated with hysteria and with disturbances of the female pelvic organs. Amenorrhea is not always a factor, but is a frequent symptom of this syndrome.

Wherever the disease has its local manifestations a vasodilator as nitroglycerin, seems to be of benefit. Whether there is too little thyroid secretion or too much suprarenal secretion, or whether there is an insufficient ovarian secretion (and thyroid extract stimulates the ovaries), certain it is the administration of thyroid extract is generally of benefit.

Diagnosis. Ordinarily mild cases of this disease are not difficult to diagnose, that is, the "dead fingers" and icy cold hands and feet. Also easy of diagnosis are the severe cases in which there is gangrene of some part of an extremity, especially when it occurs in young individuals and is symmetrical. Obliterating endarteritis or advanced arteriosclerosis is likely to occur only in individuals who are old, and is more likely to occur in men than in women, and peripheral gangrene from this cause is generally readily diagnosed. Embolic obstruction of some terminal vessel, with possibly gangrene, will generally show a history of some acute disease that may cause embolism or some chronic valvular disease of the heart.

Raynaud's syndrome occurs mostly in women, and will be found associated with disturbances that are well recognized as due to disturbances of the thyroid gland. It is also frequently associated with disturbances of the menstrual function. It can occur at any age, and has even been noted in young children.

The disease which at times it may simulate is erythromelalgia. This disease is rare, and was first described by Weir Mitchell in 1872 and again in 1878. He coined the word "erythromelalgia," which means "red, painful limb." As its name implies, it attacks an extremity, is painful, and the color of the part affected is bright red. The part feels hot, and cold soothes it. It is made worse by heat. The cause of the disease is unknown, though Weir Mitchell thought it might be due to an inflammation of the nerve endings.

The disease may be transient and intermittent, or it may cause more or less incapacity. Although it may stop and may not recur, no treatment seems to have any special effect upon it. In erythromelalgia the feet are more frequently affected than the hands. The condition is worse in hot weather and better in cold weather. Sometimes there seems to be an interrelation between Raynaud's syndrome and erythromelalgia, both conditions occurring in the same patient, or at least erythromelalgic symptoms may be present in a patient who has Raynaud's syndrome.

The differential diagnosis of Raynaud's syndrome from erythromelalgia may be briefly stated as follows: Raynaud's syndrome occurs at all ages; by far the majority of cases occur in females; it is likely to be symmetrical; the disturbance is increased by cold; the part attacked is more or less anesthetic and pale, or it may be livid, and may be icy cold. On the other hand, erythromelalgia generally occurs after twenty years of age; it is more frequent in males than in females; it is almost always asymmetrical; it is benefited by cold and not increased by it; the part affected is tender instead of anesthetic; it is pink or purplish in color; it is hot and the blood-flow to the part is increased.

Syringomyelia, a disease due to a gliomatous growth in the spinal cord, presents a very different set of symptoms from Raynaud's with paralysis, muscle atrophy, and some loss of sensation. The only similarity to Raynaud's syndrome is that there may be such trophic destruction that a phalanx may be lost.

Angioneurotic edema, another trophic disturbance, needs to be mentioned in this connection, because it may occur in an individual who has Raynaud's symptoms. The treatment of angioneurotic edema is very much more satisfactory than is the treatment of either Raynaud's disease or erythromelalgia. The probable cause of angioneurotic edema is a disturbance of the sympathetic nervous system affecting the vasomotor nerves, probably due to toxins in the blood, similar to those that cause urticaria, especially giant urticaria. Such a condition is probably a sort of anaphylactic reaction.

Mild ergot poisoning may simulate Raynaud's syndrome.

To sum up the diagnostic points in Raynaud's syndrome, it should be remembered that it may be very mild; that women are attacked much more frequently than men; that the commonest age is from fifteen to thirty, though no age is exempt; that frequently uterine and ovarian disturbances will be found; that the worst attacks sometimes occur periodically, with a more or less close relationship to the menstrual epoch; and that some of the well-known symptoms of a disturbed thyroid secretion are often present, probably more frequently on the side of hypothyroidism than hyperthyroidism.

It has been repeatedly stated that no treatment is of any value

in Raynaud's disease except perhaps nitroglycerin. I have found this not to be true; that treatment to stimulate a more healthy activity of the thyroid gland has been of marked benefit, especially in severe cases, such treatment being thyroid extracts and iodides. Nitroglycerin will always help the condition, and so will local hot baths. In other words, the writer believes that Raynaud's syndrome is not always incurable, and that it is due to a disturbance of the internal secretions, and probably more especially to malsecretion of the thyroid and suprarenal glands. Certain it is that treatment aimed to correct these secretions is beneficial and many times curative.

Before presenting a series of brief clinical histories of this syndrome, we wish to urge that it be recognized and never forgotten that every disease, severe in its entirety, may occur in mild forms, and "missed" cases may occur. The grades of severity of Raynaud's syndrome are as follows:

1. It may be so mild as not to be recognized. Such patients have cold hands and feet, irregular pains in various parts of the body, and they are cold in winter and hot in summer (vasomotor ataxia, as it has been termed). There may be so much contraction of the peripheral bloodvessels that the internal vessels, especially the abdominal, are dilated, and frequently diarrhea is caused, sometimes termed "intestinal sweating," from which cause a patient may have a morning diarrhea without other symptoms. Or there may be such abdominal congestion as to cause various other gastro-intestinal disturbances, albuminuria, etc. This kind of congestion or spasmodic contraction of bloodvessels is probably often the cause of ovarialgias, delayed and painful menstruation, and menorrhagia.

2. There are cases of medium severity in which there are ice-cold hands and feet, chilblains of varying degrees, sore fingers and toes, suppurations around the nails, perhaps severe headaches, and there may be erythromelalgic symptoms of red face and red hands, with or without pain. There may be faintness or syncope, dizziness, some slight nervous disturbances, as of the eyes, and recurrent albuminuria or hematuria. This condition may be one of the causes of albuminuria of adolescence and of orthostatic albuminuria.

3. Severe cases, occurring less frequently, in which there may be serious heart disturbances, deep ulcerations of the fingers and toes, serious cerebral symptoms, or severe abdominal symptoms.

4. There may occur, very rarely, such serious and uncontrollable spasms of the bloodvessels as to cause gangrene and sloughing of parts of the extremities. It is also conceivable that fatal heart attacks may be caused by this syndrome.

The following clinical histories will demonstrate the varying types and varying severity of this peculiar syndrome:

CASE I.—A girl, aged fifteen years, was first seen on February 3, 1915. She began a year ago to have attacks of the hands becoming

icy cold and turning blue, and at the same time she feels very faint. The attacks last about twenty minutes, even with rubbing and with plunging the hands into hot water. These attacks are becoming more frequent. Her feet are always cold and her hands are generally cold, but during these attacks they are ice-cold. Menstruation began nine months ago and has been pretty regular, lasting about four days, and is normal in amount. She is a well-nourished, apparently perfectly healthy girl. Nothing abnormal was found, except that the thyroid is somewhat enlarged and presses toward the larynx, and she dislikes to have anything tight around her throat. Her voice has been a little hoarse for the last two years, and drops peculiarly, much as a boy's voice when it is changing.

Small doses of iodide did not benefit her, but thyroid extract has thus far prevented the attacks. There is no question that the thyroid gland can be enlarged and not be properly secreting or excessively secreting.

CASE II.—The following is a case of the next degree of severity: This is a stenographer, aged thirty-four years, who for years has been troubled with cold hands and feet and with chilblains of all types and degrees. The last two years especially these cold fingers and ice-cold hands with sore, swollen knuckles and sore, tender fingers have been on the increase, especially in winter. For the last year there have been repeated attacks of little infections around the finger-nails, without any history of local injury whatsoever. These particular fingers have become extra cold, extra red, painful, and finally these little ulcerations appeared. There has never been any history of real blisters. She has always been well in most every respect, except that menstruation has been more or less irregular. She is also nervous at times, gets depressed, cries easily, and is subject to headaches, mostly from eye defects; but these headaches are always aggravated at these periods of depression. The thyroid gland is decidedly enlarged on the left side, and has been for the last few months. The gland becomes smaller under iodide, but she feels much better, and the gland is softer under thyroid treatment. There are absolutely no other signs of under-secretion of the thyroid and no signs of over-secretion. As this patient has only recently come under treatment, and as the weather is growing warmer, when the fingers and hands will improve from that fact alone, the results of the thyroid treatment have not yet been determined, but she certainly feels better generally under the thyroid.

CASE III.—The following case represents another degree of intensity of Raynaud's syndrome: A married woman, aged thirty-seven years, has had poor circulation for years, and has weak heart turns. Her hands become numb, but not quite like falling asleep, she says. Often she sees only one-half of an object at a time. She frequently feels full-headed, has pain in the left side of the head in conjunction with more or less of a blind turn. With these blind

turns she is likely to have numb hands, and she cannot use her hands for some time. The hands and feet get cold during these attacks. These blind turns occurred more frequently up to two years ago than since, and they last from three-quarters of an hour to an hour. During these attacks she does not hear well, and her mind is not clear as to what people are saying, or what she herself is about to say. Her face also sometimes gets numb, expecially around the mouth. Sometimes with these attacks she gets quite short of breath, and occasionally has pain in the region of the heart. Her eyes are not the cause of her headache; they have been carefully examined and excluded. The headaches are most likely to occur just before and during menstruation. She says she never felt as well as she did during her pregnancies. This was probably due to a normally increased thyroid secretion at these times. She gets short of breath on exertion, and has palpitation at times. She has consulted a large number of physicians for the above-described condition.

She has been married thirteen years, and has two children, the youngest six years of age. She had typhoid fever seven years ago and measles followed by pneumonia two years ago. The physical examination is practically negative. The tongue is a little trembly. The pulse is 96. The systolic blood-pressure 140. There is no history of epilepsy or fits or anything pointing toward that condition. The urine is normal. The thyroid gland seems small.

Nitroglycerin helps her, but she is better under small doses of iodide and thyroid, and has had no blind attacks since that treatment was started four months ago. This case shows a tendency to irregular spasm of the bloodvessels. How much permanent help can be given her I do not yet know.

Case IV.—The next patient is a woman, aged thirty-nine years, sent to me for treatment on account of severe pain in the left side of the head and in the back of the neck and for persistent insomnia. This patient was first seen by me in April, 1914. Three years before she had had some of this trouble which lasted four or five months. Now for the last four or five months she has had it again and very much worse the last three weeks. It occurs almost daily and sometimes is very severe. She has no nausea or vomiting with it. With this pain she flushes and gets very hot. The left side of the face burns, although both cheeks look hot and red. Sometimes she aches all over, and especially the arms and shoulders ache. Her hands tremble at times, and she has some palpitation and an intermittent pulse. During these head attacks tears stream down the left cheek. On leaning over the head aches much worse. The hands are sometimes bright red, at other times dark, almost cyanosed; they are always discolored she says. The redness of the hands disappears when they are held over her head. The feet are cold, and sometimes she has to put them into hot water to stop the discomfort.

She is married and has six children, the youngest four years old. Menstruation is regular. Some years ago she had some sort of a benign growth removed from the right side of the abdomen, and the appendix was removed at the same time. She does not know just what the growth was. She had typhoid fever twenty years ago. There is no trouble in the eyes to account for her headaches. She is well nourished, slightly over-weight, and has a pendent abdomen. All physical examinations are negative. The pulse is 84; the systolic blood-pressure 125.

Thyroid extract did not benefit her. Under good doses of nitroglycerin or sodium nitrite she soon improved greatly, and by June, 1914, two months after I first saw her, she was practically well of the condition.

I did not see her again until February of this year, when she had a little return of her headache, with flushing of the face and watering of the left eye. Her hands have been all right. She was again having insomnia, and again having an intermittent pulse. She was given 1 grain of thyroid a day, as larger doses had caused disturbance before, and nitroglycerin again. She immediately improved, and has been well ever since.

CASE V.—A young boy, aged eight years, was first seen by me in 1910. He gave a history of having had a large number of intestinal attacks, diarrheas, etc., and a history of having attacks of albuminuria. He had peculiar pigmentations on different parts of his body, and many leukodermic spots. There was no specific history. Heart, lungs, abdomen, and urine were negative at the time I saw him. He had a few enlarged cervical glands. This boy was in a miserable condition, and unfit to go to school. He had been put upon all sorts of diets, and all sorts of diagnoses had been made, both in this country and in England.

I believed the condition to be a disturbance of the internal secretions, largely a subsecretion of the thyroid, and on account of the pigmentations on his skin a disturbed secretion of the suprarenals. He was given small doses of thyroid, and rapidly and continuously improved, and soon was well. But for two or three years, whenever the treatment was long discontinued, he had a return of his symptoms, but was immediately again improved on taking thyroid. The child later was able to go to school, and has become a strong boy.

This was a form of Raynaud's syndrome with vasomotor disturbance of the bloodvessels of the abdomen, causing diarrheas and recurrent albuminuria.

CASE VI.—This patient, a married woman, aged twenty-eight years, was first seen in June, 1913. She had two children, the youngest eighteen months old and the oldest three and one-half years. With the first child she had had an acute nephritis and a slight convulsion, but the kidneys soon recovered. Four months before

I saw her she had had a nervous exhaustion attack of some kind, and was said to have had a pericarditis, and was sick four or five weeks. From the time of the birth of the first child she had had no kidney trouble, and there has never been any edema. For a long time now she has been having breathless atttacks with heart storms, the heart beating very rapidly and pounding very hard. Her hands and feet are generally cold and sometimes blue, and the lips become absolutely blue. Although she is pale at times, she is not anemic; the hemoglobin content of the blood is 100 per cent. Frequently one finger gets numb and cold, and remains so for hours; sometimes it is one toe. During these attacks she has a dull ache in the region of the heart.

Examination shows the heart to be slightly enlarged, with no murmurs, no roughness, and no friction. The systolic blood-pressure is 120. The lungs are normal and the abdomen negative. The spleen is not enlarged, and there are no enlarged glands anywhere. Her hair is of a light reddish tinge, but the pubic hair is absolutely white, and she says it has always been so. Menstruation has always been regular. The tongue is normal.

At the time the patient was seen in consultation her physician feared she might die in one of these attacks. She was very weak and was confined to her room, although not absolutely to her bed.

A diagnosis of Raynaud's syndrome was made, and she was given nitroglycerin and small doses of thyroid. She had a rapid recovery, soon having no breathlessness, and gaining weight. However, if she stopped the nitroglycerin she again became breathless and had heart distress. Also, as long as she takes the nitroglycerin her hands are not cold. The date of this observation is September 10, 1913, three months after I first saw her. From that time, September, 1913, I have occasionally seen her, but she cannot go long without either thyroid or nitroglycerin treatment, although there are months when she is well and takes no medicine. If she feels cold she has learned to take the nitroglycerin and to stop it when she feels better.

In February, 1914, she was again troubled with coldness and getting blue around the mouth, was breathless, and was having pain around the heart. She was also excessively sleepy, and said that her hands and feet puffed at times, althugh there was no real edema. All of this showed subthyroid secretion. She was given 1 grain of thyroid extract twice a day and $\frac{1}{200}$ of nitroglycerin twice a day, and she again soon improved. It was noted at this time that streaks of white were coming in the hair on her head. She says that from five years of age until she was sixteen she had brown spots on her skin on various parts of the body. Also, part of the hair on the head of one of her children, she says, was at first absolutely white, but now has gradually become light brown. All of this story shows a disturbed thyroid secretion and perhaps a

disturbed suprarenal secretion, with symptoms of peripheral contraction of the bloodvessels and internal congestions, with disturbance of the heart. In other words, it is Raynaud's syndrome, and thyroid and nitroglycerin have been of marked benefit to her.

CASE VIII.—A girl, aged seventeen years, first came to me in February, 1911. She had been for two years under treatment for a peculiar mottling of the hands and feet. For four years her hands and feet had been more or less frequently excessively cold. These conditions were always worse in cold weather, but still they persisted somewhat in summertime. For the last three months she has had peculiar gastric crises, with terrible pain in the epigastric region, occurring even as frequently as once a week, associated with a chill and followed by fever. There is no nausea or vomiting and no loss of consciousness. She has had all kinds of treatments, and there have been all kinds of diagnoses. She has never had any sickness except scarlet fever and measles, and these were when she was a child. Menstruation is regular and normal. The family history is entirely negative.

Physical examination was negative in every respect; the urine and blood were also negative. She had a blister on the back of one heel, and she has had such sores on her feet frequently. Her hands were like pieces of ice, and were almost blue. She says her hands itch a great deal and perspire sometimes profusely, and the same is true of her feet even while they are icy cold. She has had blisters on both hands, off and on, more or less for four years. Sometimes these sores on her hands and feet have to be lanced, and she has had one on her heel for three months. Her legs up to her knees and her arms almost to the elbows were peculiarly mottled by dark bluish and brown spots, not ecchymotic, much as one sees when an extremity is thoroughly chilled and the blood begins again to circulate. There was no loss of sensation anywhere.

She was given nitroglycerin and thyroid extract. In a few days she had another abdominal attack, but it was milder then the previous ones. The sore on her foot soon healed and she had less perspiration of the hands and feet. She had one other attack of the abdominal pain the following month, but no severe attack, and no chill and no fever. A few blisters occasionally occurred, but she continued to improve under thyroid treatment.

In April of the same year, after two months of treatment, she had some attacks of becoming breathless and having pain in the substernal region, but the hands and feet were not nearly so cold. The heart at times was rapid, but the pulse had been over 100 from the beginning. Occasionally she had considerable pain in the left ovary, which was a neuralgia.

She continued to improve, and from July, 1911, was not seen until October, 1913, when she reported that she had been very well, though her hands were sometimes cold; but her feet did not get

cold, she never had any more of the blisters and very little of the mottling, and no chills or abdominal pain. I know she has been well since, as I frequently see her on the street. In other word the improvement of the Raynaud's syndrome in this case was remarkable.

CASE IX.—A girl, aged sixteen years, was first seen by me in consultation in 1905. The family history was negative, and there was nothing important in her previous history. She began to menstruate when she was fourteen, but had not menstruated at all during the last year, namely, from fifteen to sixteen. About a year before I saw her she had begun to have attacks of fever, dating from the time menstruation ceased. These fever attacks would last about nine days and recur in about three weeks. They were preceded by chills, headache, loss of appetite, pain in the abdomen, loose bowels, and insomnia. Various diagnoses had been made, such as hysteria, intestinal disturbance, typhoid fever, malarial fever, and Hodgkin's disease (on account of her having, during these attacks, an enlarged spleen and sometimes enlarged glands in the neck).

I saw the patient in one of these fever attacks. The glands of of both sides of the neck, of the axillæ, and of the groins were enlarged. The heart and lungs were normal. The spleen was enlarged to the umbilical line, the liver was normal in size, there were no pelvic symptoms, and the urine and blood were negative. With the history of these periodic attacks, in the absence of menstruation, I was sure that they were symptoms of some kind of a toxemia.

Although there were no signs of subthyroid secretion, except that she did not menstruate and had these symptoms of toxemia, she was given 5 grains of thyroid extract twice a day. In ten days she began to menstruate for the first time in over a year and had entirely recovered from all abnormal signs and symptoms.

Under intermittent thyroid medication she menstruated regularly for nearly a year, but after stopping this treatment she again ceased to menstruate, and after not menstruating for two months she again had a high temperature, the spleen was again enlarged, the glands of the neck were tender and enlarged, and the abdomen was tense and distended; in other words, there was a complete recurrence of the attacks of the year before.

I saw her again in consultation, and under thyroid treatment she again improved. In a few days the spleen and glands were less tender and smaller; she became apparently well and menstruated the next month.

She was then well until the following year, when she had an acute attack of tonsillitis, and again had some slight recurrence of the above symptoms. She was given thyroid, and in two or three days she was again normal. Four years following this she was still

well and had been well. This is probably an instance of Raynaud's syndrome with abdominal congestion.

CASE X.—This patient was a man, aged thirty-six years, who had various symptoms of various kinds of nervous syphilis; but there were no symptoms, and never had been, of gumma in the spinal cord or brain and no real paralysis. He was seen in a consultation on account of some of his nervous pains, supposedly due to some other condition than the syphilis. Examination of the blood showed a strong Wassermann reaction, and he was treated with salvarsan, became well, and was able to attend to his business. Before he had received any salvarsan, while he was being treated with mercury, and also when he was supposed to be cured of his syphilis, he had several attacks of being unable to talk or think, sometimes with terrible headaches, and at these times he acted like a person under the influence of some drug. Sometimes he would suddenly drop a fork or a spoon, and would mumble in his speech, but at such times he was generally able to walk. These attacks never lasted long, he never showed any paralytic symptoms. These attacks were due to sudden spasm of some of the bloodvessels in his brain and represent a species of Raynaud's syndrome associated with syphilis. An association of Raynaud's disease with syphilis has been recorded by others. Salvarsan has apparently cured him, but of course he is likely to have some recurrences from his syphilis.

CASE XI.—This patient, a girl, aged seventeen years, was first seen in 1904. She gave a history of having had peculiar sleeping attacks from July, 1903, to April, 1904. In these attacks she would be practically comatose for two or three days. They generally occurred about once a month, but lately they had occurred twice a month. There never were any convulsions, although there were some symptoms of stiffening of the muscles. Occasionally there was a little mucous froth at the mouth. In the last attack previous to my seeing her she had slept for twelve hours. After wakening from the attack for several days she could not hear, and for some days could not see. At times she was almost blind. For a time she did not recognize her family, her own clothing, or her surroundings. She appeared hardly to breathe while in these semicomatose attacks. She took no nourishment or liquid during this time, and passed no urine, sometimes for two or three days. She began to menstruate at the age of fourteen, but the flow was irregular, and generally occurred about every five weeks. These sleeping attacks since they began, have occurred just before it was normal time for the period to appear.

Physical examination was absolutely negative, except that the thyroid gland seemed a little enlarged. At this time we did not recognize the association of Raynaud's symptoms, due to the contraction of the bloodvessels of the brain with what seemed to me

like a toxemia. I did make a diagnosis of epilepsy and a cataleptic state, and gave her thyroid, believing that she needed this to combat whatever protein poisoning was in her system. The coma and cataleptic attacks entirely disappeared. She had one or two epileptic attacks, however, and later a few petit mal attacks. The menstruation became regular and on time, and the patient entirely recovered. She married in 1905, and was well until 1910, when I saw her last. There were no other symptoms in her case of subthyroid secretion, except that she did not menstruate on time, and that she had these periodic toxic attacks. I now feel sure she had Raynaud's syndrome, with the cerebral vessels affected, associated with a subthyroid secretion.

CONCLUSIONS. 1. Raynaud's disease is not a distinct entity; it is a syndrome caused by the disturbance of one or more internal secreting glands.

2. There is primarily no real disease of the bloodvessels, but the vasomotor control is so abnormally disturbed that most profound contraction of certain bloodvessels may occur in different parts of the body, perhaps more or less coincident with abnormal dilatation of other bloodvessels. If the contracted bloodvessels are peripheral the parts more or less lose their function and show various trophic disturbances.

3. This bloodvessel spasm may occur in the internal organs of the body as well as peripherally, though much less frequently and more difficult of diagnosis.

4. The syndrome is probably due to disturbances of more than one of the ductless glands of the body that have internal secretion, but there is always apparently some disturbance of the thyroid gland, perhaps a diminution of the vasodilator stuff of this gland.

5. Judiciously applied, thyroid treatment improves the majority of cases, perhaps all, and cures some cases. Nitroglycerin is always of temporary benefit and local heat is always of immediate benefit.

OBSERVATIONS ON A CASE OF FAMILY PERIODIC PARALYSIS.

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WE have to report some observations upon a case of family periodic paralysis. The case was studied very carefully, from a

neurological point of view, by Taylor[1] in 1898. The present investigations lie entirely in the field of chemical pathology.

The literature on the subject was very completely reviewed up to 1898 in Taylor's paper.

In 1901 Singer[2] gave a critical digest of the literature up to that date, with bibliography. Fairly complete bibliographies will also be found in the papers of Kramer, 1908,[3] and Gatti, 1911.[4]

Kramer counted 78 cases in the entire literature, and since that time probably not more than a dozen have been reported.

The neurological aspect of the disease has been carefully studied by a large number of observers, notably Goldflam,[5] Oppenheim,[6] Taylor,[7] Mitchell,[8] and Oddo and Darcourt.[9] A discussion of the etiology of the disease will be found in Singer's[10] and in Buzzard's[11] papers.

Pieces of muscle have been excised by Goldflam, Oppenheim, Crafts,[12] and Singer. All have described the microscopic appearances as "abnormal." Oppenheim found waxy degeneration. Goldflam and Crafts described the fibers as being hypertrophied and vacuolated, and Crafts also says that there is an increase in fibrous tissue. Singer found extensive fissuring in the cut sections which he considered an artifact, but which he thinks would not have been present unless there were "some essential abnormality in the muscle fibers to produce such uniform and unusual appearances."

The toxicity of the urine during an attack and interval have been studied of Goldflam, using Bouchard's method, who found that "during attacks there was a distinct increase in the urotoxic coefficient, the increase in some cases being nearly fourfold." This author found that the knee-jerk was diminished in rabbits after the injection of urine collected during an attack, but failed to get changes in the electrical reactions. Singer, using the same method, found that during an attack the urine was definitely more toxic than during an interval. Mitchell, also using this method, found no difference in the urotoxic coefficient before and during an attack. These findings are of purely historical interest.

[1] Family Periodic Paralysis, Jour. Nerv. and Ment. Dis., 1898, xxv, 637. Continued same, p. 719.

[2] Case of Family Periodic Paralysis with Digest of Literature, Brain, 1901, xxiv, 257.

[3] Zur Frage der Periodischen Paralyse der Extremitäten, Russische Medizinische Rundshau, 1908, vi, 454.

[4] La Paralysie Périodique, Gaz. d. höp., Paris, 1911, p. 1327.

[5] See Taylor, loc. cit.

[6] See Taylor, loc. cit.

[7] Loc. cit.

[8] Case of Family Periodic Paralysis, Amer. Jour. Med. Sci., 1899, cxviii, 513.

[9] Les réactions électriques dans la paralysie familiale périodique, Archiv d'Electric. Med., 1902, xi, 1.

[10] Loc. cit.

[11] Three Cases of Family Periodic Paralysis, Lancet, London, 1901, ii, 1564.

[12] Fifth Case of Family Periodic Paralysis, Amer. Jour. Med. Sci., 1900, cxix, 651.

The toxicity of the blood serum was studied by Mitchell and by Mitchell, Flexner, and Edsall,[13] but the results were apparently negative.

Crafts has extracted from the feces during an attack a toxic substance which, when injected into rabbits and guinea-pigs, produced a transient paralysis. He does not appear to have controlled his results. Two authors, Mitchell and Mailhouse,[14] on attempting to draw blood for examination found that it clotted with great rapidity, but did not determine the coagulation time by any accurate method.

Upon the urine a large amount of work has been done. Mitchell has made analyses of total nitrogen, urea, uric acid, sulphur, and phosphates, but does not give the diet in detail, so that the significence of the results is uncertain. Crafts found an increase in ethereal sulphates during an attack, but he also fails to record the diet. The same is true of Singer's complete analyses.

Mitchell, Flexner, and Edsall[15] determined the total nitrogen of the food and urine and of ammonia and creatinin in the urine, the latter by the old Neubauer-Salkowski method (before Folin's method was published), which is undoubtedly far from accurate. The ammonia was continuously low, and the creatinin was very low for a day or two before attacks, and during the first part, and rising sharply, just after or during the latter part of the attacks.

Holtzapple[16] made a large number of urinary examinations, urea and indican being the chief things recorded. The diet is not mentioned, nor the method for determining urea. In general (average of a large number of cases), he found that the urea elimination seemed below normal and the indican increased.

Mailhouse has found a striking reduction in calcium and magnesium in spite of the fact that his patient was on a liberal diet containing more or less milk. He also found in the urine on several occasions a proteose-like body which decreased during attacks, and in addition practically always found creatin in the urine. The creatinin was somewhat higher just before the attack rather than afterward, as in Mitchell, Flexner, and Edsall's case. The methods used are not given, nor is the diet recorded in detail. Several authors have mentioned a high indican test during attacks; the same has been found to be true in our case.

Atwood[17] found in one of his cases that the intestinal flora contained a marked preponderance of the Bacillus aërogenes capsulatus.

In regard to the ordinary blood examination, moderate leukocytosis has been found by Goldflam, Taylor, and by Singer.

[13] Physiological and Chemical Study of Three Cases of Family Periodic Paralysis, Brain, 1902, xxv, 109.

[14] Observations on a Case of Family Periodic Paralysis, Jour. Nerv. and Ment. Dis., 1910, xxxvii, 209.

[15] Loc. cit. [16] Family Periodic Paralysis, Penn. Med. Jour., 1903, vii, 408.

[17] Family Periodic Paralysis, New York State Jour. Med., 1913, xii, 579.

The most recent papers on this disease are those of Gardner,[18] who reports a typical case, and discusses the etiology and treatment, and of Diller and Rosenbloom,[19] who studied the nitrogen, sulphur, calcium, magnesium, phosphate, and fat metabolism during an interval only.

Gardner believed the condition to be due to an intoxication, and on that hypothesis treated his patient by catharsis, low protein diet, avoidance of alcohol, together with caffein, digitalis, and bromides during an attack, and got marked improvement.

The only positive findings of Diller and Rosenbloom were a marked decrease in creatinin and an increase in undetermined nitrogen. The average creatinin coefficient was 4.8.

CASE REPORT.—The clinical data on our case are as follows:

J. T. S., male, aged thirty-five years; weight 83.6 kilograms.

The disease has been in the family for five generations; the history is absolutely typical, namely, attacks of complete flaccid paralysis of all the skeletal muscles save those of the face, of deglutition, and of the eye muscles, lasting from six to forty-eight hours, and coming on at irregular intervals, the longest interval being seldom over six days, the sphincters and diaphragm not being involved, the reflexes and electrical reactions being diminished, or abolished during the height of the more severe attacks, and the patient being perfectly well in the intervals. Normal respiration was not involved in the paralysis, but the accessory muscles apparently were, for during the more severe attacks the patient was unable to take a deep inspiration or make a forcible expiration.

A complete genealogy showing the line of descent and the afflicted members in each generation is given in Taylor's paper.[20] Since the appearance of that paper a case has arisen in the sixth generation, a niece of the patient, aged nine years, having had several rather mild but characteristic attacks.

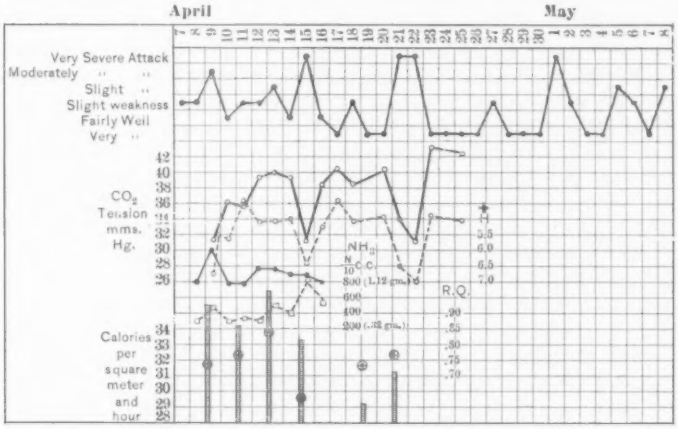
The patient came to the hospital at our request merely for purposes of investigation. He was in the medical wards from April 7 to May 8, 1914. During this time he had a number of attacks, some severe and some mild. The sequence and severity of the attacks are indicated in the accompanying chart. Those of April 15, April 21–22, and of May 1, were severe, there being complete paralysis of the arms, legs, trunk, and neck muscles, lasting twelve hours or more. Several other attacks, lasting a shorter period, and in which the paralysis was less complete, likewise occurred.

A complete clinical description of the attacks is also given in Taylor's paper, and since during the present stay in the hospital the attacks were entirely similar, it will be unnecessary to go into details here.

[18] Case of Periodic Paralysis, Brain, 1913, xxxv, 243.
[19] Family Periodic Paralysis, Arch. Int. Med., 1914, xiv, 869.
[20] Loc. cit.

The physical examination save for an enlarged spleen (felt two fingers' breadth below the costal margin, with increase in splenic dulness) was negative. The skeletal muscles were unusually well developed, so much so in fact that the possibility of a pseudo-muscular hypertrophy was suggested. However, since the patient had a perfectly normal degree of muscular ability, being in fact rather athletic, taking much exercise, such as bicycle riding, swimming, and bowling, between attacks, this was ruled out.

Several writers have described dilatation of the heart, increase in pulse rate, and other signs of cardiac weakness during attacks. No evidence of any such occurrence was found in our case.



The upper curve indicates the patient's condition as regards paralysis from day to day. The CO_2 tension by the Plesch method is shown by solid lines and circles; by the Lindhard method, broken lines and circles. The ammonia in cubic centimeters of a N/10 solution and also in grams is shown by broken lines and squares; the hydrogen ion concentration of the urine by solid lines and dots; the respiratory quotients by circles containing crosses, and the basal metabolism in calories per square meter and hour, by perpendicular columns. The first four basal metabolism determinations are with the Benedict, the last two with the Douglas apparatus.

The urine was negative to ordinary examination save for a rather high amount of indican, which increased during attacks. This increase may not improbably be explained by the constipation which always occurred with the attacks.

There never was any albumin except after the administration of large doses of sodium bicarbonate, and the presence of albumin, under such circumstances, cannot be considered abnormal.[21]

There were never any sugar, urobilogen, or acetone bodies.

[21] Palmer, W. W., and Henderson, L. J., Clinical Studies on Acid Base Equilibrium, Arch. Int. Med., 1913, xii, 153.

The most recent papers on this disease are those of Gardner,[18] who reports a typical case, and discusses the etiology and treatment, and of Diller and Rosenbloom,[19] who studied the nitrogen, sulphur, calcium, magnesium, phosphate, and fat metabolism during an interval only.

Gardner believed the condition to be due to an intoxication, and on that hypothesis treated his patient by catharsis, low protein diet, avoidance of alcohol, together with caffein, digitalis, and bromides during an attack, and got marked improvement.

The only positive findings of Diller and Rosenbloom were a marked decrease in creatinin and an increase in undetermined nitrogen. The average creatinin coefficient was 4.8.

CASE REPORT.—The clinical data on our case are as follows:

J. T. S., male, aged thirty-five years; weight 83.6 kilograms.

The disease has been in the family for five generations; the history is absolutely typical, namely, attacks of complete flaccid paralysis of all the skeletal muscles save those of the face, of deglutition, and of the eye muscles, lasting from six to forty-eight hours, and coming on at irregular intervals, the longest interval being seldom over six days, the sphincters and diaphragm not being involved, the reflexes and electrical reactions being diminished, or abolished during the height of the more severe attacks, and the patient being perfectly well in the intervals. Normal respiration was not involved in the paralysis, but the accessory muscles apparently were, for during the more severe attacks the patient was unable to take a deep inspiration or make a forcible expiration.

A complete genealogy showing the line of descent and the afflicted members in each generation is given in Taylor's paper.[20] Since the appearance of that paper a case has arisen in the sixth generation, a niece of the patient, aged nine years, having had several rather mild but characteristic attacks.

The patient came to the hospital at our request merely for purposes of investigation. He was in the medical wards from April 7 to May 8, 1914. During this time he had a number of attacks, some severe and some mild. The sequence and severity of the attacks are indicated in the accompanying chart. Those of April 15, April 21–22, and of May 1, were severe, there being complete paralysis of the arms, legs, trunk, and neck muscles, lasting twelve hours or more. Several other attacks, lasting a shorter period, and in which the paralysis was less complete, likewise occurred.

A complete clinical description of the attacks is also given in Taylor's paper, and since during the present stay in the hospital the attacks were entirely similar, it will be unnecessary to go into details here.

[18] Case of Periodic Paralysis, Brain, 1913, xxxv, 243.
[19] Family Periodic Paralysis, Arch. Int. Med., 1914, xiv, 869.
[20] Loc. cit.

The physical examination save for an enlarged spleen (felt two fingers' breadth below the costal margin, with increase in splenic dulness) was negative. The skeletal muscles were unusually well developed, so much so in fact that the possibility of a pseudo-muscular hypertrophy was suggested. However, since the patient had a perfectly normal degree of muscular ability, being in fact rather athletic, taking much exercise, such as bicycle riding, swimming, and bowling, between attacks, this was ruled out.

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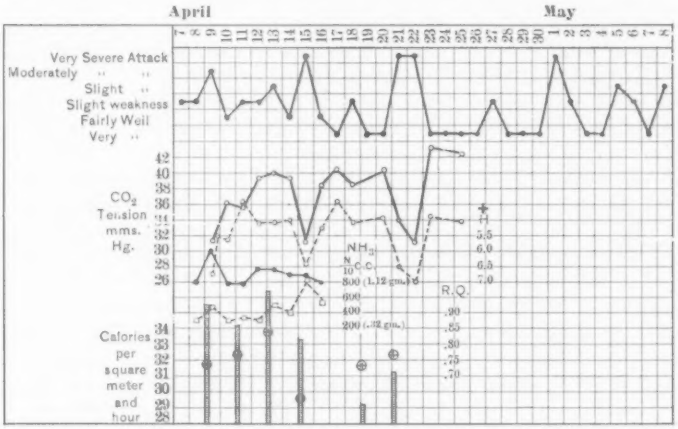

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[21] Palmer, W. W., and Henderson, L. J., Clinical Studies on Acid Base Equilibrium, Arch. Int. Med., 1913, xii, 153.

Blood smear was negative. Wassermann test on the blood was negative.

EXPERIMENTAL OBSERVATIONS.—The findings of Goldflam, Oppenheim, and Taylor that the electrical reactions of the muscles are diminished or abolished during attacks suggest at once that the abnormality lies in the muscle itself or the end plate rather than in the nervous system. Such an abnormality might be produced by an alteration in the intermediate metabolism of the muscle cell or by some disorder of general metabolism leading to the elaboration of some circulating toxin having some special action upon muscle.

With a view to gaining information on the second alternative we have carried out the following investigations:

First of all we determined the basal metabolism. The determinations of April 9, 11, 13, and 15 were made with the Benedict respiration apparatus. The method has been described and the significance of basal metabolism discussed in a previous paper by one of us (J. H. M.).[22] The determinations of April 19 and 21 were made with a type of respiration apparatus devised by C. G. Douglas,[23] in which the expired air is collected in a rubber bag and analyzed. The gaseous exchange was determined in each of these experiments by five periods of five minutes each, on the apparatus. The figures for CO_2 and O_2 in the five periods were averaged and the calory output determined by indirect calorimetry.[24] With both types of apparatus the patient was examined in the morning during complete muscular rest, and in the *nüchtern* condition. The results of these experiments are shown in the chart. The metabolism is expressed as calories per square meter of body surface per hour. The body surface was calculated from Meeh's formula.[25]

With a view to finding out whether any acidosis occurred during the attacks, the alveolar carbon dioxide tension was determined daily from April 9 through April 23. Two methods were used: (1) Four of the so-called B samples of Lindhard were taken and the results averaged. The method has been described by Lindhard.[26] (2) A determination by the Plesch method[27] was made. The Lindhard method gives the CO_2 tension of the arterial, the Plesch of the venous blood. The Plesch determinations, therefore, are always a fewer millimeters higher than the Lindhard, but should show similar fluctuations if an acidosis is present.

[22] Studies of Basal Metabolism in Obesity and Pituitary Disease, Jour. Med. Research, 1915, xxvii, 121.

[23] Jour. Physiol., vol. xlii; Method for Determining Respiratory Exchange, Proc. Phys. Soc., 1911, vol. xvii.

[24] Williams, Riche, and Lusk, Animal Calorimetry II, Jour. Biol. Chem., 1914, xii, 349.

[25] Body surface $= 2.3\sqrt[3]{\text{weight}^2\ (\text{grams})}$.

[26] Excitability of Respiratory Centre, Jour. Physiol., 1911, xlii, 343. See also Krogh, A., Apparatus for Study of Muscular Work, Skand. Archiv. f. Physiol., 1913, xxx, 383.

[27] Hämodynamische Studien, Ztschr. f. Exper. Path. u. Therap., 1909, vi, 380.

An inspection of the results which are given in the chart will show a striking fall in both sets of samples occurring with the attacks of April 9, 15, and 21 to 22.

These drops in CO_2 tension at once suggested that an acidosis was present during attacks, so certain other tests were carried out to throw further light on the subject, but unfortunately failed to do so.

The hydrogen ion concentration of the urine was determined by the method of Henderson and Palmer.[28] In the attack of April 9 it increased from 6.5 to 5.5, but showed no rise in that of April 15.[29]

The titratable acid in the urine was not increased during the attacks.

The urinary ammonia showed a rise in the attacks of April 15, but not in that of April 9.

The response to alkali both during intervals and attacks was normal, namely, after the ingestion of 5 grams of sodium bicarbonate, marked decrease in the hydrogen ion concentration occurred within two hours, and was accompanied by a decrease in the ammonia, apparently corresponding to that found in normal individuals.[30]

Determinations of the lactic acid in the blood and in the urine, both during an attack and in an interval, were made by Ryffel's method.[31] The results were all within normal limits. The blood varied from 10 to 21 mgm. per 100 c.c. and the urine from 11 to 16 mgm. per twenty-four hours.

An attempt to find further evidence of an acidosis was also made by determining the dissociation curve of CO_2 free blood by Barcroft's method.[32] This constitutes a test for an excess of non-volatile acids in the blood. The results were negative; specimens of blood taken both during an attack and interval gave approximately the same percentage saturation when exposed to an atmosphere of 17 mm. of oxygen tension, the figure being 62 per cent. interval, 58 per cent. in an attack; the normal limits given by Barcroft being from 65 per cent. to 75 per cent.

The total nitrogen and creatinin in the urine showed nothing abnormal. On a purin-free diet the total nitrogen in the urine was from 10 to 13 grams per day. The creatinin showed no changes during attacks as compared with the intervals. It was regularly about 1.5 grams per day. Creatin was occasionally present both

[28] Intensity of Urinary Acidity, Jour. Biol. Chem., 1913, xiii, 393.

[29] We are indebted to Dr. Palmer for the hydrogen ion determinations, the ammonia and titratable acidity of the urine and the lactic acid determinations on blood and urine.

[30] Henderson, L. J., and Palmer, W. W., Extreme Variation of the Concentration of Ionized Hydrogen in Human Urine, Jour. Biol. Chem., 1913, xiv, 81.

[31] Method for Lactic Acid in Urine, Journ Physiol., vol. xxxix; Proc., p. 5.

[32] Lewis, Ryffel, Wolf, Cotton, and Barcroft, Dyspnea in Cardiac and Renal Patients, Heart, 1913, v, 45.

during attacks and in the intervals, being from 0.1 to 0.2 grams per day.

The blood showed a high non-protein nitrogen content. Three observations, two during an attack, one during an interval, showed the same result, 74 mgm. per 100 c.c. Uric acid and urea were retained in such proportion as would be expected with the degree of nitrogen retention. Creatinin was absent from the blood during one attack and during the interval was present within normal limits.[33]

The sulphonephenolphthalein excretion was normal during an interval, 61 per cent. in an hour and ten minutes.

Indican was nearly always present in the urine and showed a marked increase during attacks, but on a low protein diet there was but a trace, except during an attack, when it again increased.

The patient was seen again on January 9, 1915. After leaving the hospital in May, at our advice (because of high blood nitrogen), he went on a low protein (no meat) diet and remained on the same until the middle of September. During this period he was singularly free from attacks; never stayed in bed later than 11 A.M. all summer. In the fall he returned to a general diet and has continued it ever since. From October 15 to November 15 he had several rather mild attacks. Since then he has been better than ever in his life. Three-quarters of the time he has been up at 7 A.M. and never has been in bed later than noon. In the latter part of November he began to work on a steady job (outdoor salesman), a thing he has never done before.

A specimen of blood was examined for non-protein nitrogen, on this visit of January 9, 1915, and was found approximately the same as when in the hospital, 67 mg. per 100 c.c. of blood. The urine contained a moderate amount of indican, otherwise was negative.

DISCUSSION. Of the above observations, the fall in CO_2 tension is by far the most striking. Since the curves taken by two entirely different methods are in close agreement we feel that they are perfectly reliable. The possible known explanations for a fall in the CO_2 tension are the development of an acidosis and an increased sensitivity of the respiratory centre.

The latter might be produced by the stimulating action upon the centre of some circulating toxin. The methods used in searching for other evidence of an acidosis proved negative, except that in one attack there was an increase in the hydrogen ion concentration of the urine and in another, a rise in the ammonia. No evidence was found for supposing it to be a lactic acidosis. The Barcroft test showed no evidence of an increase in the non-volatile acids in the blood. The reaction to alkali being normal both during

[33] We are indebted to Dr. W. Denis for the nitrogen and creatinin determinations in the urine and blood.

attacks and intervals is strong evidence against an acidosis in the ordinary sense. As mentioned above, there never were any acetone bodies in the urine.

We therefore are strongly inclined to the hypothesis that the fall in CO_2 tension is due to an increased sensitivity of the centre, and the most likely cause for this would seem to be an intoxication of some sort.

In regard to the basal metabolism it will be noticed that the results with the Douglas apparatus are both lower than any with the Benedict apparatus. This is undoubtedly the result of a systematic error with the Douglas apparatus, due to a decreased ventilation of the lungs, since the subject breathes against a slightly increased pressure. However, the two Douglas experiments should be comparable one with another, though not with those done by the Benedict method.

The experiments (both methods) were all quite satisfactory with the exception of that of April 15, in which the different periods were not in close agreement and the R. Q. gave an impossible value, being below 0.7. The R. Q.'s in all the other experiments were between 0.78 and 0.88, which is as close as is often obtained on different days in the same individual. Disregarding then the experiment of April 15, we find that the basal metabolism determined with the Benedict apparatus on April 9 and 13 (days on which there was an attack) was higher than on April 11, when he was fairly well. Also, that in the case of the Douglas experiments, that of April 21, a severe attack, gave a higher value than that of April 19, when he was unusually well. In other words, the basal metabolism of this patient is apparently higher during attacks than in the intervals. This is rather extraordinary, for one would expect the metabolism to be lower during the enforced, and hence more complete muscular rest present while the patient is paralyzed. This increase in metabolism might reasonably be interpreted as being a further bit of evidence in favor of an intoxication.

The retained non-protein nitrogen in the blood is interesting, but we are at a loss to explain it. The urine showed no evidence of nephritis; there was no cardiac hypertrophy or hypertension, and the 'phthalein excretion was normal. It is also of interest to note that the retained nitrogen persisted after eight months, although during that time there had been marked improvement in the periodic palsy.

The creatinin in the urine showed no change during attacks, as was found in the case reported by Mitchell, Flexner, and Edsall.[34] The creatinin coefficient was 6.6, which is nearly up to the normal low limit of 7 given by Shaffer.[35] Hence the low coefficient found by Diller and Rosenbloom[36] is not a constant feature in this disease.

[34] Loc. cit.
[35] Excretion of Creatin and Creatinin, Amer. Jour. Physiol. 1908, xxiii, 1.
[36] Loc. cit.

No definite conclusions can be drawn from these scattered observations. We think, however, enough positive findings were obtained to make it seem probable that this disease is one of metabolism and not of nervous origin. The question of acidosis is certainly worthy of further study,[37] and the hydrogen ion concentration of the blood might yield valuable information. We had not the facilities for performing this test.

Gardner's case showed a striking improvement on eliminative treatment and low protein diet. Also in our case an improvement dated from the time he began such a diet, though when he returned to a general diet the improvement continued. It is only fair to bear in mind that many observers have reported a tendency for this disease to improve with age, so it is quite possible that J. T. S.'s improvement was part of the natural sequence of events and had nothing to do with the low protein diet.

We should hardly agree with Diller and Rosenbloom, who thought that their patient's freedom from attacks while in the hospital was due to the low protein diet that he was getting. He had just had a very severe attack; in our patient's case after a very severe attack he is nearly always unusually well for a week or so. We do believe, however, that a low protein diet is worthy of a trial, and may, over a long period of time, have some influence over the number and severity of the attacks.[38]

THE ROLE OF SYPHILIS IN HYPERTENSIVE CARDIOVASCULAR DISEASE.[1]

By Henry Farnum Stoll, M.D.,

ASSISTANT PHYSICIAN TO THE HARTFORD HOSPITAL, HARTFORD, CONN.

The steadily increasing mortality from diseases of the cardiovascular system at a time when the deaths from the communicable diseases are decreasing, is a problem of great seriousness. The victims, for the most part, are not from the ranks of the aged who have run their course, but from those who have just attained that

[37] The patient has for several years been in the habit of taking potassium citrate when he felt an attack coming on. He is not certain whether it ever did any good.

[38] At the suggestion of Dr. W. B. Cannon, the effect of adrenalin was tried in one attack; the tendency of adrenalin to lessen the fatigability of muscle being the point in mind. Adrenalin 1 to 1000 solution ♏xv, was given subcutaneously every hour for three doses. The blood-pressure was raised 12 mm., but no change at all was found in the paralysis.

The effect of physostigmin was also tried in an attack. Gr. $\frac{1}{150}$ was given every hour for four doses (subcutaneously). This also failed to have any apparent effect on the paralyzed muscles.

[1] Read before the Hartford Medical Society, April 5, 1915.

period of life when they should be of the greatest value to the family and the State.

That it is a question for serious thought the recent statistics of Louis I. Dublin,[2] of the Metropolitan Life Insurance Company, clearly show.

In the ten years ending with 1910 the mortality from cerebral hemorrhage and apoplexy had increased to 18.8 per cent.; that from organic diseases of the heart, 39.3 per cent. The deaths from Bright's disease showed an increase of 18.1 per cent., and most astounding of all the mortality from disease of the arteries had risen from 5.2 to 25.8, or 396.2 per cent.

An important factor, probably the determining factor in this vascular degeneration, is the strenuous life we lead in this country, where "step lively" is the watchword. But will overwork alone account for this? A perfectly constructed motor, properly cooled and oiled, will run a long time at high speed. But an imperfection in a bearing, a piston ring that binds, or a loose connecting rod, spells disaster.

To the abuse of alcohol, the poison of lead and lues, and hard labor, most of the arterial changes are attributed. While definite knowledge, in spite of much experimental work, is very meager, it is probable that there are a considerable number of toxins, endogenous and exogenous, that exert a deleterious effect on our cardiovascular tissue.

It has been recognized for many years that syphilis shows a marked predilection for the arteries; but it was not until the advent of the Wassermann reaction and the more recent luetin test of Noguchi that it became possible to ascertain its real importance. With a few exceptions the possibility that congenital lues might be the underlying cause in some of the hypertensive cases occurring in middle life does not appear to have been considered by writers on this subject.

In the discussion of a case of congenital syphilis, reported by Messenger[3] in 1871, which showed at autopsy an interstitial nephritis, it was suggested that such a condition might prove to be the starting-point of a nephritis in later life.

Southerland and Walker[4] found at autopsy on an infant of sixteen months, whose father had had lues and died of heart disease, an endarteritis of the cerebral arteries and an interstitial nephritis. They agree with Guthrie, whom they quote, that it is probable that both congenital and acquired syphilis plays an important role in the interstitial nephritis of the adult. Hintzelman[5] shares this view. Cassel[6] found renal changes in ten out of twelve infants with congenital lues who came to necropsy.

[2] American Journal Public Health, 1913, iii, 1272.
[3] Quoted by Armstrong, British Med. Jour., 1914, i, 958.
[4] British Med. Jour., 1903, i, 959. [5] Zeitschr. f. Kinderh., 1913, ix, No. 1.
[6] Quoted by Power and Murphy, System of Syphilis, Oxford University Press, 1908, i, 358.

In a recent paper[7] I have cited several cases with hypertension, which were apparently associated with a prenatal syphilitic infection. The material for this article comprises four groups of individuals and being so divided, attacks the problem of cardiovascular disease from somewhat different angles.

The first comprises fifty patients seen in office and consultation work, and for the most part represents individuals who experienced but slight inconvenience from this condition and were not incapacitated from their duties.

The second group is made up of one of the terminal stages of arterial disease, viz., the apoplectics. The third group, a very small one, consists of widows whose husbands had died from one of the above causes. The fourth comprises individuals, one of whose parents either has some cardiovascular-renal disorder, or had died from apoplexy, sudden cardiac failure or "kidney trouble."

GROUP I.—There were in all 50 cases, all white, with a systolic pressure over 160. Thirty-five (70 per cent.) were women, 15 (30 per cent.) were men. This sex distribution is almost the exact opposite of Janeway's[8] statistics. In his series of 458 cases the males were 67 per cent. Nettleship,[9] however, found that of eighty children under thirteen years of age with interstitial nephritis, 64 per cent. were females against 36 per cent. males; and this is in accord with Sawyer,[10] whose 40 cases of interstitial nephritis under thirteen years of age showed 69 per cent. females and 31 per cent. males. In parenchymatous nephritis in children Nettleship found the males slightly in excess.

None of the cases in this series suffered from lead poisoning, but two had used alcohol to excess. The cases of Group I can, with considerable exactness, be placed into one of three classes.

A. Those who either admit a primary lesion or who are known to have lived in intimate association with one who had syphilis or whose children exhibit some manifestations of hereditary lues.

B. Those individuals who, denying a venereal infection, had either a family history of cardiovascular disease (often the sudden death of parent in early life) or whose history suggested congenital syphilis, whether in the patient or in some other member of the family.

C. Patients whose history suggests neither acquired nor hereditary syphilis.

Such a classification is open to criticism because of obvious possibilities or error. Thus Case 11 had been very devoted to a dipsomaniac brother, who had acquired syphilis and who now has a strongly-positive Wassermann. Her opportunities for infection

[7] Stoll, Jour. Amer. Med. Assoc., 1914, lxiii, 1558.
[8] Archiv. Int. Med., 1913, xii, 755.
[9] Trans. Ophth. Soc., iii, 51. Quoted by Sawyer, vide No. 16.
[10] St. Thomas' Hospital Reports, 1906, xxxv, 459.

were probably many, yet she not only gives no history suggestive of primary or secondary manifestations, but her ill health very definitely antedates the time of her brother's infection. Accordingly she is classed as an acquired case, though it is quite possible that it was an hereditary one, as both of her parents died of "kidney trouble."

In like manner Case 41, placed in Class C, might be with some reason grouped with those probably exposed to syphilis, as her husband died from pernicious anemia. Acknowledging these limitations, this division, nevertheless, has much that is suggestive.

Taken as a whole the Wassermann test was made on 42 of the cases in this group, with 33⅓ per cent. reacting positively. The luetin test was used in 45 cases, 82 per cent. of whom were positive. In subdivision A of Group I are 17 individuals for the most part with a good family history, who either admit having had syphilis or were presumably exposed to infection in the family, or who have children exhibiting some signs of a congenital infection.

The Wassermann was positive in 61.5 per cent. of these cases and the luetin test in 76 per cent.

It is subdivision B of this group which consists of individuals from families prone to cardiovascular disease that I desire especially to draw your attention. There are 19 patients in this class and the Wassermann was positive in only 12 per cent., while the luetin test was positive in 89 per cent.

Neither the Wassermann nor the luetin test was positive in 17 cases, or 89 per cent., and one who reacted negatively to both tests (Case 28) is undoubtedly of specific origin, as will be evident when the history is reviewed in detail.

C. In the fourteen cases whose personal history does not suggest an acquired infection and whose family history is not that of cardiovascular disease the Wassermann was positive in 33⅓ per cent., and the luetin in 82 per cent. It is quite likely that these were chiefly acquired cases notwithstanding the negative history.

For years neurologists have recognized that syphilitic infection in certain families tends to be manifest by various disorders of the nervous system; thus a husband may be tabetic, the wife paretic, and certain children exhibit paresis or possibly cerebral syphilis. In one family mentioned by Nonne[11] paresis was present in three generations. There is much from the clinical stand-point to suggest a strain of spirochetes with special affinity for nervous tissue, and Nichols[12] has isolated a strain which appears to have this property. A study of the cases here presented suggests there is a type of familial cardiovascular syphilis. While the occurrence of these lesions in parent and child might be explained by the inheritance of poor vascular tissue, this would not explain the occurrence

[11] Syphilis and the Nervous System (English translation), 1913.
[12] Jour. Amer. Med. Assoc., 1914, lxiii, 466.

in both husband and wife of cardiovascular syphilis. It remains to be seen if there exists a strain of spirochete with special affinity for vascular tissue.

An instance of familial cardiovascular degeneration, of which syphilis appears to be the cause, is the following:

The grandparents died from cardiac disease, an uncle in early life of apoplexy, and an aunt suddenly from heart disease. One living aunt had had several strokes of apoplexy, and her unmarried sister gives a positive luetin test, though a negative Wassermann. Two of the third generation are unmarried—middle-aged women with hypertension. One gave a positive luetin with a negative Wassermann. In the other both tests were negative, but as a girl she had a persistent ulceration of the rectum which was followed by a stricture that required removal. One brother who knows of no infection gave a positive luetin test, another is stated to have a chronic ulcer near his anus and to "shed the soles of his feet" periodically. A third brother died suddenly of heart disease when sixteen years old. In view of the family and personal history the sister with hypertension in whom both the Wassermann and the luetin tests were negative is classed as luetic. The mother of this generation died suddenly of cardiac dilatation following pneumonia, and the presumption seems warranted that she probably had a syphilitic myocarditis.

What we might term "the syphilitic lead" in the history of Case 21 is not so much that both parents and a sister died from nephritis, as the fact that the patient and two of her sisters all became deaf in early womanhood without apparent cause. Insidious deafness is a common result of congenital lues. It is noteworthy that the highest pressure (270 to 280 auscultatory, wide cuff) was in a woman with an hereditary infection. Only once have I met with a higher pressure, and that was in an unmarried woman, aged forty-nine years, whose mother, aged sixty-nine years, had died of a "shock," though she had her first stroke several years before. In this woman the systolic pressure was 300, diastolic 160, and there was an accompanying aortitis and nephritis. It seems quite possible that this was an inherited syphilis also. The further history of this case is of interest. She developed a tonsillar diphtheria one week after I saw her, and though she had antitoxin promptly, she died in about a week from cardiac failure; the pressure steadily fell until the end.

Several of these cases would not have been detected except for my custom of examining, whenever possible, the parents of patients suspected of having hereditary syphilis. In one instance the mother of a young man with interstitial keratitis was found to have a blood-pressure of over 160.

In another case the father of an anemic child with a positive Wassermann and of two children who were deaf and dumb was

found to have hypertension and a strong luetin reaction. In a third instance the mother of a girl who had precordial pain, had an aortitis and systolic blood-pressure of 194. The mother's sister also had aortic disease with a systolic pressure of 220.

Case 31 is of interest, as mercury and salvarsan are theoretically contra-indicated with marked kidney involvement. Notwithsatanding that the patient had diabetes and eliminated only a trace of 'phthalein in two hours, she experienced much symptomatic relief from three injections of neosalvarsan and a course of mercury injections combined with the iodide of potassium. She was first given mercury by mouth, then by injection, and as no untoward effects were noted, neosalvarsan was finally administered. The amount of 'phthalein eliminated a year later was over 15 per cent. The blood-pressure was lower and the patient felt much better. The Wassermann is still very positive, though the general condition is good, except for glycosuria.[13]

A woman, aged forty-two years, consulted me because of increasing weakness and a thoracic pain which she feared might be due to pulmonary disease. There was nothing to be found in her lungs, but her systolic pressure was 170, diastolic 115. The Wassermann reaction, even with fortified antigens was negative. Upon questioning her husband I learned that he had an initial lesion twenty-two years previously, for which he had received practically no treatment. He was married sixteen years ago and four years later he had a recurrence of mucus patches and sore throat which subsided after a few weeks' medication.

He considers himself in perfect health, but his Wassermann is strongly positive and both he and his wife gave a marked luetin reaction.

Of especial interest in this case is the fact that an innocent infection may take place years after the chancre from recurring mouth lesions. It also demonstrates that apparent health is compatible with an active syphilitic infection as revealed by the Wassermann test.

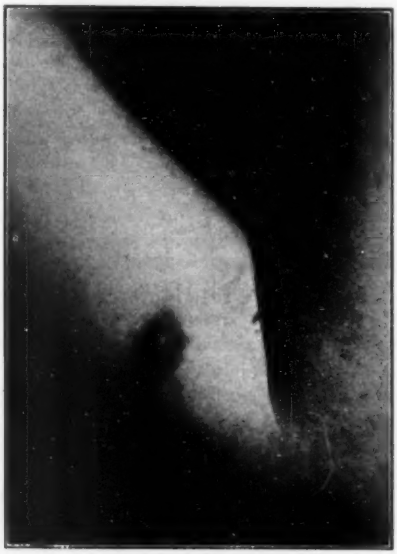
The accompanying illustration shows the wife's luetin reaction, and is typical of the average reaction obtained in this series. In three or four cases, however, the resulting pustule was very much larger than the one shown here.

While it is true that a high percentage of hypertensive cases are suffering from interstitial nephritis, Gull and Sutton asserted years ago that similar changes could be found in the smaller arteries throughout the body, though they were usually most marked and easiest of demonstration on the kidney. This conception of hypertensive disease, as a condition affecting the smaller arterioles throughout the body, is the one generally accepted today.

[13] The day proof was corrected she died after being comatose three days. Excellent health up to first convulsion. *Urine* loaded with sugar.

In some of these cases the examination of the urine suggested a small granular kidney; in the majority it was negative. Several were given the 'phthalein kidney function test and the results are recorded in a separate column. For the most part good function is shown.

GROUP II.—The cases of apoplexy, fifteen in all, were nearly all patients in the Hartford Hospital, and in only a few could any history be obtained, owing to their mental condition. Six were under sixty and nine were older. The oldest was a hale old man of ninety-one, who made an excellent recovery from a slight shock.



Positive luetin reaction in woman with hypertension whose Wassermann was negative. In addition to the pustule there is a well-marked areola. Both the Wassermann and luetin tests were positive in the husband.

He had an initial lesion nearly fifty years before, though he remembered no secondaries. His leutin test was definitely positive. Of the group under sixty, 20 per cent. gave a positive Wassermann reaction and 83 per cent. a positive luetin. Only one of the older group had a Wassermann, and it was negative. The luetin was positive in 55 per cent. of those over sixty. This group is so small that one would be unwarranted in concluding that the same percentage would obtain in a large series. It demonstrates, however, that syphilis is a very common factor in apoplexy, irrespective of age.

The spinal fluid was examined in five cases of apoplexy. In several there was a slight cellular increase and a positive globulin test with a negative Wassermann reaction and a positive luetin. The Wassermann in blood and spinal fluid agreed in all cases. In most instances only 0.2 c.c. of fluid was used; with larger amounts the percentage of positive Wassermann's would probably have been somewhat higher. Two cases were of specially interest as showing the difference between an acquired infection and one that was presumably congenital. A man, aged fifty years, with a right hemiplegia, was referred to me by Dr. E. A. Wells. He had had a chancre some years before. The Wassermann in both blood and spinal fluid was very positive, and in the latter there was a marked globulin increase; cells not counted. The other, a man aged thirty-six years, with a left hemiplegia, was seen with Dr. Cantarow. He denied absolutely any venereal infection and the arch of his palate was exceedingly high and narrow, which is almost pathognomonic of hereditary lues. The blood and spinal fluid Wassermann reaction was negative, though 1 c.c. of fluid was used. There was no cellular increase and no globulin. Both patients exhibited a strong luetin test.

GROUP III.—It was my privilege to test seven widows whose husbands died from cardiovascular or renal disease in middle life. The Wassermann was done in six, and was positive in half (50 per cent.); the luetin test was positive in all (100 per cent.), though in one in whom the Wassermann was very strong it did no develop until the sixth week.

GROUP IV.—Group IV is made up of thirty-seven individuals, children and adults who knew of no venereal infection, and who either gave a history of parental death from heart disease, apoplexy, or "kidney trouble" (usually in early life), or had a parent living with one of the above maladies. The latter were few. Twelve of this group were included in the Class B of Group I. Thirty-four, or 89 per cent., gave either a positive Wassermann or luetin reaction. Many appeared to be in good health, but the majority had some complaint, and in a number of instances symptomatic improvement followed syphilitic treatment. I do not consider this percentage as fairly estimating the amount of hereditary lues in cardiovascular families. As nearly a third of the cases were patients who came for examination because of some evidence of ill health, this percentage would have undoubtedly been lowered considerably if the number of apparently healthy individuals studied had been greater. In a previous study of syphilitic families irrespective of health, I found 59 per cent. to be infected, and of those who appeared to be perfectly healthy, the luetin test was positive in 39 per cent.

Furthermore, it by no means follows that the various symptoms complained of by this group were in each instance due to lues,

solely because the Wassermann or luetin test was positive. The patient with aortitis may have gall-stones, or the stomach symptoms may be due to cancer, even though lues is admitted. Nor are we justified in assuming that in all of this group the infection was hereditary because no history of infection could be obtained. Granting these limitations, the fact remains that a large percentage of the offspring of cardiovascular parents have a prenatal infection. (See Case 10.)

It is probably true, and indeed most fortunate, that syphilitic infection does not always mean clinically syphilitic disease. By this I mean that an infection may be more or less dormant for years and finally die out without in any way appreciably affecting the health of its host or shortening his life. But while admitting this possibility, we have as yet no means of ascertaining in which case this will happen and in which disaster will follow.

Most of the Wassermann tests in this series were made by Mr. R. V. Story at the laboratory of the State Board of Health, which is under the direction of Prof. Conn, of Wesleyan. A number were done by Dr. Jessie Fisher at the State Hospital at Middletown, one in the laboratory of Dr. J. A. Fordyce, of New York, and several by Drs. Russ and Brayton, of this city. The luetin was very kindly supplied by Dr. Noguchi, of the Rockefeller Institute.

Cholesterinized antigens were employed in thirteen cases, and their more general use would have given a somewhat higher percentage of positive results. Nevertheless, several negative results were reported from each of the four laboratories in late congenital cases when the luetin test was positive; this was obtained several times even when fortified antigens were used. Provocative injections of salvarsan would undoubtedly have increased the number of cases exhibiting a positive Wassermann, but even if the reaction remains negative, lues cannot be absolutely excluded. The luetin reactions were for the most part of unusual severity, probably due to the fact that the patients were, as a rule, given a small amount of potassium iodide for a time previously. This seems to "activate" the test even better than mercury or salvarsan.

The luetin test has been used about 10,000 times, Dr. Noguchi tells me, by over 100 different observers, and with but very few exceptions all agree that the test is specific for lues; as specific in fact as the tuberculin test for tuberculosis.

Kaliski,[14] testing Hebrews at the Montefoire Home, questioned the specificity of the papular type of reaction. It seemed incredible to him that so many orthodox Hebrews could have a latent syphilitic infection, especially in the absence of the more common signs of syphilitic disease.

As a matter of fact, syphilitic disease, especially of the aorta, is

[14] New York Med. Jour., 1913, xcviii, 24.

very common in this race. That in many cases the luetin test may be an indication of an hereditary infection is a possibility that has so far received insufficient consideration.

In a few instances where "activation" with mercury and potassium iodide was omitted before giving the test the reaction was papular in type and of moderate severity, while the Wassermann was very positive. Emory,[15] Wilson,[16] and others have drawn attention to the fact that in the late manifestations of hereditary syphilis the luetin test is more often positive than the Wassermann.

Vedder and Borden,[17] comparing the Wassermann and the luetin test in a series of over 700 individuals in whom they employed cholesterinized antigens, say "it is apparent that in tertiary latent and treated cases the luetin test is apparently more efficient in detecting syphilis than the most efficient Wassermann." Eighty per cent. of the patients tested by Borden and Vedder were between fifty and eighty years of age, and suffered from the various degenerative processes that attend that period of life. The combined results of the Wassermann and the luetin test revealed the fact that over 45 per cent. had been infected with syphilis.

Valuable as the Wassermann and the luetin tests are in the diagnosis of obscure cases, it is very unfortunate when they are used as short cuts to diagnosis, as neither test is infallible. It takes less time to obtain blood for the Wassermann reaction than it does to go over the family and personal history with a fine tooth comb, as it were. A carefully obtained history may be supplemented but not supplanted by either the Wassermann or luetin test.

TREATMENT.—In addition to the usual regime adopted in these cases it was possible to observe the effect of specific treatment on several patients. The number is altogether too small, however, to draw any conclusions as to the relative value of the different forms of antiluetic treatment. Mention has been made of the great improvement in a patient with aortitis and diabetes who was excreting only a trace of 'phthalein in two hours.

I am far from being sure that salvarsan is indicated in all cases. Sometimes an important military position can be taken by a long siege where an assault would fail. Several patients have exhibited very satisfactory improvements in subjective symptoms, usually coincident with some lowering of the blood-pressure following several months of mercury injections combined with potassium iodide by mouth. Inunctions give satisfactory results, but their field of usefulness is limited in private cases.

Mercury by mouth has not seemed to be so efficacious. The urine of these patients has been carefully watched and rarely has there been signs of kidney irritation. In four instances the kidney func-

[15] Lancet, 1914, i, 223.
[16] Quoted by Armstrong, vide note 2.
[17] Vedder and Borden, Jour. Amer. Med. Assoc., 1914, lxiii, 1750.

tion was determined before treatment was instituted and several months later. The results are shown in the following table.

TABLE SHOWING PHENOLSULPHONEPHTHALEIN ELIMINATION.

Before treatment.					After treatment.				
Case No.	Date.	Per cent. 1st hour.	Per cent. 2d hour.	Total per cent.	Date.	Per cent. 1st hour.	Per cent. 2d hour.	Total per cent.	Medication used.
23	June 4, 1913	22	7	29	Feb. 3, 1915	47	22	70	Hg. injections; KI.
25	July 1, 1914	29	20	49	Feb. 21, 1915	56	20	76	Hg.; neosalvarsan and salvarsan.
47	May 5, 1914	39	10	49	Feb. 4, 1915	32	25	57	Hg. injections; KI.
39	Jan. 21, 1914	Trace	Trace	Trace	About June 15, 1914	Trace	Trace	less than 10	Hg. mouth; Hg. injection; neosalvarsan; KI.
					Feb. 22, 1915	Trace	15	15	

Two cases might be cited as illustrating the possibilities and limitations of specific therapy:

A married woman, aged sixty-five years (Case 23), was referred to me by Dr. Frederick Crossfield because of dyspnea. There was marked pulsation in the carotids, and the systolic pressure was 190 and diastolic 85. Rest in bed and purgation enabled her to lie comfortably with head low, but when she began to get about again in two weeks the pressure rose to over 160. For the next three months she was given injections of mercury, at first the biniodide, grain $\frac{1}{6}$, twice a week, and later the salicylate, grain $\frac{1}{10}$ weekly, together with KI by mouth. Her improvement has been most gratifying. Last summer, after a morning of "canning," her pressure was 140 and once since then was 130, though it averages about 160. Three Wassermanns were negative, but the luetin test was very strong. The increase in the 'phthalein output after several months' treatment is shown in the preceding table.

In contradistinction to this is the young woman whose systolic pressure was 270. When she had as much improvement as could be expected from the usual dietetic-rest-hot bath regime, she was given three injections of neosalvarsan and a number of mercury, though the family was told it was questionable if any improvement would follow. In the months succeeding the treatment she seemed to have a little more endurance and was much brighter. Her speech, which had been thick, improved considerably. A cough that had persisted for many months, accompanied by purulent sputum in which tubercle bacilli were never found, completely disappeared. The systolic blood-pressure remained, however, at about 270, and I cannot feel that the treatment was of any great benefit. In view of the extensive structural changes that attend such high pressure it does not seem reasonable to expect any treatment to avail. Had it been possible to have detected her syphilitic infection

in her childhood as it would be today, and had she received a thorough course of treatment through a period of several years, this tragedy of middle life might have been avoided. By promptly stamping on the fuse a calamity may be averted. After the explosion there are only tears and regrets.

The results of this investigation can be summarized as follows:

1. Syphilis is the underlying or basic factor in a much higher percentage of hypertensive cases than has hitherto been realized. Of 50 individuals studied 90 per cent. either gave a positive Wassermann or luetin test, or were known to have had lues, or had children with hereditary syphilis.

2. Nineteen were from cardiovascular families. In seventeen of them either one or both test were positive. One of the two with negative reactions is surely specific. This strongly suggests the existence of what might be termed "familial cardiovascular syphilis."

3. It would seem that hypertensive disease is one of the most common—possibly the most frequent—of the so-called "late" manifestations of hereditary syphilis.

4. Apoplexy and sudden cardiac death occurring in middle life are almost always due to syphilis, and it cannot be considered a negligible factor even in the aged.

5. The remaining parent and the children of individuals dying a cardiovascular-renal death in middle life should be tested for syphilis as they are infected in a high percentage of cases.

6. Specific treatment has given very satisfactory results in a few cases for the most part individuals whose systolic pressure was under 200. The careful administration of mercury over a period of several months has not appeared to be injurious to the kidney even when there was considerable reduction of 'phthalein output. In a few instances the kidney function was increased several months after treatment.

7. The luetin test, especially if activated by a week of mixed treatment, is often of more value than the most sensitive Wassermann in detecting these late manifestations of syphilitic infection.

TABLE I.—CASES WITH AN ACQUIRED INFECTION (CLASS A).

CASE 1.—Male, aged fifty-nine years. *Diagnosis*—hypertension; systolic, blood-pressure, 195; diastolic blood-pressure, 85. *Personal History*—had syphilis years ago; perforation of nasal septum. *Wassermann:* + +.[18] *Luetin*—not done.

[18] Wassermann reactions showing 50 per cent. inhibition are reported +. Those exhibiting more complete inhibition (75 per cent.) and the completely positive reaction, ++. The use of cholesterinized antigens indicated by *. The luetin test + signifies a papular reaction; ++ pustular; the very strong reaction, +++.

CASE 2.—Male, aged fifty-three years. *Diagnosis*—hypertension; systolic blood-pressure, 200. *Family History*—wife had several miscarriages; one child with hare-lip and imperforate anus. Family history good. *Personal History*—denies lues; alcoholic. *Wassermann:* +.* *Luetin:* +− and again + −.

CASE 3.—Female, aged fifty years. *Diagnosis*—hypertension; systolic blood-pressure, 184; diastolic blood-pressure, 120. *Family History*—husband, general pains; son, hypertension and high, narrow palate with luetin, +. Daughter very narrow palate with Wassermann strongly positive. *Wassermann:* −.* *Luetin:* −.

CASE 4.—Female, aged forty years. *Diagnosis*—hypertension; systolic blood-pressure, 195; diastolic blood-pressure, 110. *Family History*—husband has positive Wassermann. *Wassermann:* ++.* *Luetin*—not done.

CASE 5.—Female, aged sixty-two years. *Diagnosis*—aortitis; syphilis of liver (autopsy); systolic blood-pressure, 180. *Family History*—negative. *Personal History*—husband had "soft chancres" a short time before marriage. *Wassermann*—not done. *Luetin:* + + +. *Kidney Function*—first hour 22, second hour 11, total 33 per cent.

CASE 6.—Male, aged forty-seven years. *Diagnosis*—aortitis, paresis; systolic blood-pressure, 190; diastolic blood-pressure, 120. *Personal History*—chancre twenty-five years ago. *Wassermann:* + +. *Luetin:* −.

CASE 7.—Male, aged thirty-eight years. *Diagnosis*—hypertension; systolic blood-pressure, 170. *Personal History*—eleven years ago had gonorrhea; no chancre; "rash" several weeks later. *Wassermann:* ++. *Luetin:* +++. *Kidney Function*—first hour 55, second hour 25, total 70 per cent.

CASE 8.—Female, aged fifty-eight years. *Diagnosis*—aortitis; systolic blood-pressure, 170; diastolic blood-pressure, 80. *Personal History*—husband dropped dead, aged twenty-seven years. *Wassermann:* −. *Luetin:* ++. *Kidney Function*—first hour 60, second hour 25, total 85 per cent.

CASE 9.—Female, aged forty-nine years. *Diagnosis*—aortitis; systolic blood-pressure, 190; diastolic blood-pressure, 85. *Personal History*—husband had some "disease" when married, and at once had wife start to take some medicine. *Wassermann:* −. *Luetin:* +++.

CASE 10.—Female, aged thirty-eight years. *Diagnosis*—hypertension; systolic blood-pressure, 165; diastolic blood-pressure, 100. *Personal History*—husband died of "shock," aged thirty-five years. *Wassermann:* + +. *Luetin*—at first negative; at end of six weeks +. A son and daughter have positive Wassermann; a second daughter, a positive luetin test.

CASE 11.—Female, aged forty-three years. *Diagnosis*—hypertension; systolic blood-pressure, 180; diastolic blood-pressure, 110.

Family History—father and mother died of nephritis. *Personal History*—a brother had a chancre several years ago. He is very alcoholic, and sister has been very devoted to him. The brother has a Wassermann reaction positive at present. *Wassermann:* ++. *Luetin:* +++.

CASE 12.—Female, aged fifty-two years. *Diagnosis*—hypertension; systolic blood-pressure, 210; diastolic blood-pressure, 110. *Personal History*—husband had syphilis. Son has a syphilitic arthritis with luetin, +. Daughter, Wassermann, ++. *Wassermann:* +−.* *Luetin:* ++.

CASE 13.—Female, aged forty-two years. *Diagnosis*—hypertension; systolic blood-pressure, 170; diastolic blood-pressure, 115. *Personal History*—husband had syphilis before married and a positive Wassermann now. Sore throat recurred afterward. Only pregnancy a miscarriage. *Wassermann:* −. *Luetin:* ++. *Kidney function*—first hour 40, second hour 10, total 50 per cent.

CASE 14.—Male, aged fifty-two years. *Diagnosis*—diabetes; systolic blood-pressure, 170; diastolic blood-pressure, 110. *Personal History*—son and daughter deaf and dumb, another daughter anemic with positive Wassermann. Sexually promiscuous. *Wassermann*—not done. *Luetin:* ++.

CASE 15.—Female, aged fifty-five years. *Diagnosis*—hypertension; systolic blood-pressure, 195; diastolic blood-pressure, 140. *Personal History*—son had angina (mild) with Wassermann, −. Luetin, +, cured by "606" and Hg.; daughter has severe headaches. *Wassermann:* −.* *Luetin:* +++.

CASE 16.—Female, aged fifty-seven years. *Diagnosis*—aortitis; interstitial nephritis; systolic blood-pressure, 200. *Personal History*—daughter had optic neuritis; heart block; relief followed specific treatment. Wassermann. Luetin, ++. Son had headache. Wassermann, negative; luetin, +. *Wassermann*—not done. *Luetin*—not done.

CASE 17.—Female. *Diagnosis*—hypertension; systolic blood-pressure, 170+. Dactylitis with necrosis. *Family History*—one stillbirth, two miscarriages, several children died young. Daughter had severe headache with Wassermann −, and Luetin +.

TABLE II.—CASES PRESUMABLY OF HEREDITARY TYPE (CLASS B).

CASE 18.—Female, aged thirty-eight years. *Diagnosis*—aortitis; systolic blood-pressure, 180. *Family History*—two brothers died from heart disease, aged forty-five and fifty years. *Personal History*—husband knows of no venereal infection. *Wassermann*—not done. *Luetin:* ++.

CASE 19.—Male, aged fifty-three years. *Diagnosis*—aortitis; systolic blood-pressure, 210; diastolic blood-pressure, 110. *Family History*—father dropped dead, aged forty-six; a twin brother

dropped dead, aged forty-eight; a sister living has "heart trouble;" mother died, aged seventy-six, of arterial sclerosis. *Personal History*—knows of no venereal infection. *Wassermann*—after 0.45 neosalvarsan, −. *Luetin:* +++.

CASE 20.—Male, aged fifty-eight years. *Diagnosis*—aortitis; systolic blood-pressure, 242; diastolic blood-pressure, 142. *Family History*—father died, aged forty-eight, of erysipelas. Sister[1] died from an obscure abdominal lesion. Sister[2] died from a "cerebral lesion?" Sister[3] died with mental symptoms, and for years had arthritis deformans. Brother[1] lived one day. Brother[2] has had "muscular rheumatism" for years; no lues but a positive luetin test. *Personal History*—no venereal infection. *Wassermann*—after neosalvarsan, −. *Luetin:* +++. *Kidney Function*—first hour 15, second hour 15, total 30 per cent.

CASE 21.—Female, aged forty-five years. *Diagnosis*—hypertension; systolic blood-pressure, 162; diastolic blood-pressure, 106. *Family History*—father and mother died from nephritis, also one sister. A brother and sister have hypertension. Another sister has a positive luetin test. All three sisters became deaf in early womanhood. *Wassermann:* +. *Luetin:* ++. *Kidney Function*—first hour 60, second trace, total 60 per cent.

CASE 22.—Male, aged fifty-seven years. *Diagnosis*—hypertension; systolic blood-pressure, 180; diastolic blood-pressure, 110. *Family History*—father died from "shock," aged sixty-eight. Mother died at forty-five, cause? *Personal History*—no venereal infection. *Wassermann:* −. *Luetin:* +++.

CASE 23.—Female, aged sixty-five years. *Diagnosis*—hypertension; systolic blood-pressure, 190. *Family History*—father died young; cause? very alcoholic; mother died young. *Personal History*—always neurotic; first pregnancy a miscarriage. Husband has had no venereal disease. *Wassermann:* −. *Luetin:* +++. *Kidney Function*—first hour 22, second hour 7, total 29 per cent. See Table.

CASE 24.—Male, aged forty-eight years. *Diagnosis*—hypertension; systolic blood-pressure, 220. *Family History*—mother died at sixty-four, of kidney disease. *Personal History*—no venereal infection. *Wassermann:*−. *Luetin:* ++. *Kidney Function*—first hour 26, second hour 13, total 39 per cent.

CASE 25.—Female, aged forty-five years. *Diagnosis*—hypertension; systolic blood-pressure, 220; diastolic blood-pressure, 120. *Family History*—mother died at thirty-two, of heart disease. *Personal History*—for several years has had joint pains. *Wassermann*—two laboratories. *Luetin:* ++. *Kidney Function*—first hour 29, second hour 20, total 49 per cent.

CASE 26.—Male, aged forty-eight years. *Diagnosis*—aortitis; systolic blood-pressure, 208; diastolic blood-pressure, 120. *Family History*—father very alcoholic; mother died at forty-eight, cause?

Personal History—knows of no venereal infection; slight shock one year ago. *Wassermann*—not done. *Luetin:* +.

CASE 27.—Female, aged forty-three years. *Diagnosis*—hypertension; systolic blood-pressure, 280; diastolic blood-pressure, 140. *Family History*—marked family history of cardio-arterial disease. See text. *Wassermann:* −. *Luetin:* ++. *Kidney Function*—first hour 27, second hour 17, total 44 per cent.

CASE 28.—Female, aged forty-five years. *Diagnosis*—hypertension; systolic blood-pressure, 170. *Family History*—sister of No. 27. *Personal History*—persistent rectal ulceration as a girl. *Wassermann:* −. *Luetin:* −. *Kidney Function*—total for two hours 55 per cent.

CASE 29.—Female, aged fifty-three years. *Diagnosis*—aortitis; systolic blood-pressure, 194; diastolic blood-pressure, 110. *Family History*—sister has aortitis; husband died of heart disease; daughter has angina and a very positive Wassermann. *Wassermann:* −.* *Luetin:* ++.

CASE 30.—Female, aged forty years. *Diagnosis*—aortitis; systolic blood-pressure, 220; diastolic blood-pressure, 110. *Family History*—sister of preceding. *Wassermann:* +−.* *Luetin:* ++.

CASE 31.—Female, aged sixty years. *Diagnosis*—hypertension; systolic blood-pressure, 180 to 220. *Family History*—father died at fifty, of heart disease; brother of Bright's disease at sixty-eight; brother of shock at sixty-eight. *Wassermann:* −.* *Luetin:* ++.

CASE 32.—Female, aged forty-four years. *Diagnosis*—hypertension; systolic blood-pressure, 162; diastolic blood-pressure, 110. *Family History*—father died at sixty-four with Bright's disease of many years' duration; sister died of Bright's disease, aged fifty-three. *Personal History*—never strong; "growing pains" severe in childhood; "chronic fatigue." *Wassermann:* ++.* *Luetin:* ++.

CASE 33.—Female, aged forty-six years. *Diagnosis*—arthritis of knee; hypertension; systolic blood-pressure, 160; diastolic blood-pressure, 80. *Family History*—for as many years as she can remember her mother had leg ulcers; all the children's teeth were "soft" and very poor. *Personal History*—the arthritis was markedly improved by specific treatment. *Wassermann:* − *Luetin:* ++.

CASE 34.—Female, aged fifty-four years. *Diagnosis*—hypertension; hypertrophic arthritis; systolic blood-pressure, 190. *Family History*—father had a stroke at about fifty-five; mother had heart disease for years; died at seventy. A daughter has had very severe headaches for years. *Personal History*—had some psychosis several years ago. *Wassermann:* −.* Luetin −.

CASE 35.—Female, aged forty-three years. *Diagnosis*—hypertension; systolic blood-pressure, 200+. *Family History*—mother living; heart and kidney disease for many years. *Personal History*—severe growing pains when girl. Skin over patellæ very "horny" for years. *Wassermann:* −.* Luetin ++.

CASE 36.—Male, aged forty-eight years. *Diagnosis*—aortitis; hypertension; systolic blood-pressure, 230; diastolic blood-pressure, 135. *Family History*—mother died of shock at eighty; brother died suddenly at thirty-five years; had had severe headaches for years; sister has albuminuric retinitis; another sister very severe headaches. *Personal History*—denies lues; hemiplegia five months before. *Wassermann:* negative. *Luetin:* ++.

TABLE III.—UNCLASSIFIED CASES WHO GIVE NO HISTORY SUGGESTING ACQUIRED INFECTION AND WHO HAVE GOOD FAMILY HISTORIES (CLASS C).

CASE 37.—Female, aged sixty-three years. *Diagnosis*—arterial sclerosis, aortitis and mitral stenosis; systolic blood-pressure, 169 (autopsy). *Family History*—husband died at fifty-six of "Bright's disease." *Wassermann*—after neosalvarsan, −. *Luetin*: +++.

CASE 38.—Female, aged sixty-seven years. *Diagnosis*—hypertension of over ten years' duration. Systolic blood-pressure, 200. *Family History*—negative. *Wassermann:* −. *Luetin:* −. *Kidney Function*—in 2 hours over 60 per cent.

CASE 39.—Female, aged fifty years. *Diagnosis*—aortitis; diabetes; nephritis. Systolic blood-pressure, 165; diastolic blood-pressure, 115. *Family History*—husband died at sixty-two of heart disease. *Wassermann:* ++. *Luetin:* ++. *Kidney Function*—first hour trace, second hour trace. See Table.

CASE 40.—Female, aged seventy years. *Diagnosis*—hypertension; arthritis. Systolic blood-pressure, 210. *Family History*—husband has angina; denies lues. Daughter "weakling," with Luetin, +. *Personal History*—has had several slight shocks. *Wassermann*—not done. *Luetin:* +. Probably belongs in Class A.

CASE 41.—Female, aged fifty-four years. *Diagnosis*—chororetinitis; systolic blood-pressure, 200+. *Family History*—husband died at age of fifty-seven of pernicious anemia. *Personal History*—twenty years ago lost sight of right eye; three months ago left eye began to fail. *Wassermann:* −. *Luetin:* ++.

CASE 42.—Male, aged forty-three years. *Diagnosis*—hypertension; systolic blood-pressure, 160+. *Family History*—daughter has intermittent claudication. *Personal History*—denies lues. *Wassermann:* −. *Luetin:* ++.

CASE 43.—Male, aged fifty-one years. *Diagnosis*—nephritis; paroxysmal hemoglobinuria; systolic blood-pressure, 170+. *Family History*—daughter of poor mental development; very nervous; high palate. Strong luetin reaction. *Personal History*—denies lues. *Wassermann:* −*. *Luetin:* +.

CASE 44.—Female, aged fifty-three years. *Diagnosis*—aortitis; systolic blood-pressure, 170; diastolic blood-pressure, 70. *Wasser-*

mann: ++.* *Luetin:* −. *Kidney Function*—first hour 50, second hour 18, total 68 per cent.

CASE 45.—Female, aged sixty years. *Diagnosis*—carcinoma of liver and gall-stones. Systolic blood-pressure, 172; diastolic blood-pressure, 90. *Family History*—negative. *Wassermann:* −. *Luetin:* −.

CASE 46.—Male, aged fifty-eight years. *Diagnosis*—detached retina; hypertension; systolic blood-pressure, 185. *Family History*—brother at thirty-eight had slight "stroke." He had no known venereal lesion. *Personal History*—no venereal infection. *Wassermann:* −. *Luetin:* ++.

CASE 47.—Female, aged sixty-one years. *Diagnosis*—aortitis; systolic blood-pressure, 190; diastolic blood-pressure, 85. *Family History*—husband has angina, though he denies lues. *Wassermann*—later. *Luetin:* ++. *Kidney Function*—first hour 39, second hour 10, total 49 per cent.

CASE 48.—Male, age about fifty years. *Diagnosis*—aortitis; systolic blood-pressure, 200; diastolic blood-pressure, 100. *Personal History*—denies infection. *Wassermann:* ++. *Luetin*—not done.

CASE 49.—Female, aged forty-eight years. *Diagnosis*—hypertension; systolic blood-pressure, 184; diastolic blood-pressure, 84. *Personal History*—husband a drunkard; suicide. *Wassermann:* +.* *Luetin:* +.

CASE 50.—Female, aged sixty-four years. *Diagnosis*—hypertension; systolic blood-pressure, 200+. *Family History*—hypertension for ten years; negative. *Personal History*—negative *Wassermann*—not done. *Luetin:* ++.

LATENT SYPHILITIC INFECTION OF THE LUNGS.

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THE only type of pulmonary syphilis about which there is a general agreement is that seen in newborn syphilitic children. In this form of the disease, gummata may occur, but, as a rule, they are rare. The typical lesion is that known as white pneumonia. The lung presents on section a dry, smooth surface, grayish or yellowish white in color, resembling closely the cut surface of the pancreas. The process may occur in scattered patches throughout both lungs or may involve the entire lobe. This type of pulmonary syphilis is, for the most part, of pathological interest only.

In acquired syphilis most writers describe two main types of the disease as it occurs in the lungs, namely, the formation of gummata or an extensive cellular infiltration which leads to fibroid changes. If the disease assumes the indurative type, and this is by far the most common form, it usually originates at the hilus of the lung and extends outward along the bronchi and bloodvessels. The process is usually unilateral, and at most involves only a portion of one lobe; if several lobes are implicated it is the portions which adjoin the root of the lung.

In addition to these types a focal form has been described in which the lesion consists of an area of consolidation and catarrh. It is usually situated around the root of the lung, but may occur at one apex.

Whether the disease manifests itself in the form of gummata as a diffuse fibrosis or as a focal lesion, most of the cases reported indicate that the base of the lung or the area about the hilus, rather than the apex, is the part most frequently attacked. This fact is usually cited as one of the strong differential points between syphilis and tuberculosis. The general opinion has been that the apices are rarely involved, but it would be rather surprising, in view of the wonderfully diverse forms in which the localization of syphilis manifests itself, if the upper portions of the lungs should always escape.

We believe that pulmonary syphilis of a latent type occurs far more frequently than is usually supposed. The form to which we wish to call attention is that in which the localization occurs in the apices of the lungs. This type of the disease may simulate early pulmonary tuberculosis so closely as to deceive us entirely. How closely the two diseases may resemble each other is illustrated by the following cases:

CASE I (Phipps Institute, No. 9485).—Female, aged twenty-eight years, first came to the Phipps Institute June 10, 1911. Her first pregnancy had resulted in a miscarriage. She gave a history of having had repeated attacks of blood-spitting for five years. During the two years prior to her coming to the dispensary she had lost thirty pounds in weight, and for a year had had a cough, considerable greenish expectoration, and night sweats. She also complained of pain posteriorly over the base of the right lung. There was a slight elevation of temperature, 99° to 100° F.

EXAMINATION. There was some flattening beneath the right clavicle, diminished expansion, impairment of resonance on percussion, and bronchovesicular breathing.

She was sent to a sanatorium and remained away for several months, where she gained about sixteen pounds in weight, but the pulmonary symptoms remained unchanged. On her return to the Phipps Institute her sputum was repeatedly examined for tubercle bacilli as well as other organisms, but always with a negative result.

Guinea-pigs inoculated with her sputum were killed after an interval of several months, and showed no evidence of tuberculosis. At the end of ten months her condition, aside from some gain in weight, was about the same as when first seen. A Wassermann test taken at this time was strongly positive. She was then given salvarsan, followed by mixed treatment, which was continued for months. Following the salvarsan the symptoms at once began to improve, and she has apparently made a complete recovery. Three subsequent Wassermann tests have been negative. During the past year she has given birth to a healthy child. At the present time (May 15, 1915) she weighs 188 pounds, and is entirely free from pulmonary symptoms.

CASE II (Phipps Institute, No. 9617).—Male, aged thirty-three years, husband of the previous case. First visited the Phipps Institute July 6, 1911, stating that he had had a cough and greenish-colored expectoration for the past two years. He also complained of pain posteriorly over the base of the right lung. He had lost weight and had a slight elevation of temperature in the afternoon.

EXAMINATION. Patient was quite anemic. Expansion was diminished beneath the right clavicle, the percussion note was impaired, and the breathing bronchovesicular, with a harsh, prolonged expiratory sound.

He was also sent to a sanatorium, and remained away for six months. Although he gained forty pounds in weight the pulmonary symptoms persisted, and in addition his sputum was blood-streaked at times. On his return to the Phipps Institute his sputum was repeatedly examined for tubercle bacilli and other organisms and also inoculated into guinea-pigs, but with negative results. A Wassermann test taken about a year from his first visit was found to be strongly positive. The administration of salvarsan and later mixed treatment caused a disappearance of his pulmonary symptoms. At the present time (May 15, 1915) he is apparently in perfect health.

CASE III (Phipps Institute, No. 4050).—Male, aged twenty-nine years, was first seen in the dispensary of the Phipps Institute April 7, 1906. He came because of loss of weight, dyspnea on exertion, and morning cough and expectoration. On several occasions the sputum had been blood-streaked.

The family history was negative. He admitted having had gonorrhea eight years previously, but denied ever having had syphilis.

EXAMINATION. When first seen there were fine crackling rales at both apices, but otherwise the pulmonary signs were negative. The heart was normal. The sputum was negative.

This patient was seen at intervals during the next two years, and for a period of two months, in 1908, was treated in the wards

of the Institute. During his stay in the hospital the temperature chart showed frequent elevations, ranging from 99° to 99.3° F. While in the hospital he was given three injections of tuberculin. Following the third injection of 10 mg. there was a slight elevation of temperature. While his symptoms and general condition remained unchanged the rales at the apices had disappeared. The sputum continued to be negative for tubercle bacilli. On leaving the hospital he returned to the dispensary on several occasions, and then ceased to come. After an interval of four years he again reported March 30, 1915. His weight was the same as when last seen. He still had slight fever, and the morning cough and expectoration persisted. In addition he complained of nocturnal pain in his arms and hands and attacks of substernal pain and dyspnea. He had been married about a year when first seen in 1906. In the intervening nine years his wife had given birth to six healthy children.

The physical examination at this time showed no abnormality in the lungs. There was, however, a diastolic murmur at the aortic area. Believing this to be syphilitic in character a Wassermann test was made, which proved to be strongly positive. This case is of special interest because of the long duration of the pulmonary symptoms and the latent character of the trouble.

CASE IV (Phipps Institute, No. 13391).—Female, aged thirty-four years, first visited the Phipps Institute August 20, 1914. Her family history was negative. She had been married eleven years and had had three miscarriages. No living children. There was no history of an initial lesion or of secondaries. She came to the dispensary because of a cough, greenish-colored expectoration, night sweats and some loss in weight. In addition she complained of precordial pain, which had been present intermittently for six years. For four years she had suffered from attacks of burning and tingling in the legs.

EXAMINATION. Some flattening beneath the right clavicle, impairment of the percussion note, and bronchovesicular breathing. Heart was negative. The reflexes were exaggerated.

During the first six months she was under observation the night sweats, morning cough, and expectoration persisted, and the sputum was blood-tinged on one occasion. There was also a slight rise in temperature. The sputum was negative for tubercle bacilli. In February, 1915, she first complained of nocturnal headache. This gradually became worse, and finally was so severe as to interfere with her sleep. The Wassermann test was strongly positive. Under mixed treatment the headache was relieved. Later, following the administration of salvarsan, the cough ceased and the amount of expectoration was greatly reduced.

CASE V (seen in consultation).—This patient was a young male who, when first seen, had been gradually losing weight for

three months; during this time he had a slight, hacking, and unproductive cough. He was anemic, had a slight afternoon rise in temperature, and in addition had marked malaise.

EXAMINATION. At the right apex there was slight diminution in expansion, some impairment of the percussion note, and a feeble respiratory murmur.

The case seemed to be clearly one of incipient pulmonary tuberculosis, and he was accordingly advised to spend the winter at a health resort. He returned six months later with his general health improved in every way, but in the course of a few months his symptoms began to return. At this time his physician noted that the sternal end of the right clavicle was enlarged and tender. The Wassermann test was positive. After two doses of salvarsan he had no further trouble, and has remained well during the past three or four years.

It is to be noted that the symptoms in all of these cases were characteristic of pulmonary tuberculosis, namely, morning cough and expectoration, blood-streaked sputum, loss of weight, and a slight elevation of the temperature. In two there was pain resembling that occurring in pleurisy at the base of the right lung. Furthermore, they all had physical signs indicative of incipient tuberculosis.

Some years ago E. G. Janeway[1] pointed out that when the viscera became involved during the tertiary stage of syphilis there is apt to be a moderate amount of fever, a loss of weight, and night sweats. Furthermore, a careful physical examination will often reveal some other noticeable evidence of syphilis, such as enlargement and tenderness of the ribs, clavicles or tibiæ, or an enlarged or indurated testicle. Warthin[2] has emphasized the fact that next to the aorta and heart the testes are the most frequent sites of a syphilitic infection. In a pathological study of 36 cases of syphilis occurring in males, the majority of which were latent and unrecognized during life, an orchitis fibrosa was present in 31. In the case of women a history of miscarriages is extremely significant.

If the lungs are involved there is, in addition to the symptoms mentioned above, cough, which may be dry and unproductive or accompanied by a moderate amount of greenish or yellowish expectoration. Blood-streaked sputum may also occur. Pain at the base of the right lung is not infrequent and may be misinterpreted; it is usually due to a syphilitic perihepatitis and not to pleural inflammation.

The presence of latent syphilis of the lung is to be suspected if in addition to pulmonary symptoms there are present elsewhere in the body lesions which are in all probability luetic in nature, such

[1] Trans. Assoc. Amer. Phys., 1898.
[2] Ibid., 1914.

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as a periostitis, orchitis, iritis, or suspicious throat lesions. The recognition of these cases should be relatively easy.

The type of the disease which offers the most difficulty, and which for the most part, escapes detection, is that in which the symptoms are entirely pulmonary and in which there are no associated syphilitic lesions. The 5 cases we have reported were of this type. In 2 (Case I and II) we were unable at any time to detect manifestations of the disease in other parts of the body. In the other three the clinical picture in the beginning was that of tuberculosis, but the subsequent appearance of an aortitis (Case III), of nocturnal headaches (Case IV), of an osteoperiostitis (Case V), and the presence of a positive Wassermann reaction made it apparent that we had to deal with syphilis rather than with tuberculosis. The correctness of this assumption received additional confirmation in view of the fact that the symptoms were relieved as the result of the administration of antisyphilitic treatment.

The diagnosis must be made by exclusion. Thus if the symptoms and physical signs are those characteristic of tuberculosis and the sputum does not contain tubercle bacilli, or the progress of the case differs from that usually encountered in tuberculosis, the possibility of some other exciting cause should be thought of. Not only should the sputum be examined for organisms other than the tubercle bacillus, but in addition a Wassermann test should be made in every doubtful case.

The therapeutic results in these cases have been specially gratifying. In 4 the use of salvarsan was followed by an almost immediate relief of the symptoms. The remaining case has not been seen since the administration of that drug.

It is now recognized that salvarsan is much more effective in some forms of syphilis than it is in others. Skin lesions, for instance, clear up rapidly under the use of salvarsan, and the same seems to be true of pulmonary lesions.

CERTAIN PHYSICAL SIGNS REFERABLE TO THE DIAPHRAGM AND THEIR IMPORTANCE IN DIAGNOSIS.[1]

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The diaphragm, situated as it is in close relation to the intrathoracic viscera and to the upper abdomen, is involved often in

[1] Read before the Mississippi Valley Medical Association at Cincinnati, Ohio, October 27, 1914.

abnormal conditions of the organs either immediately above or below it. These conditions frequently exert a distinct effect on the physiological functions of the diaphragm, which in many cases give rise to certain definite physical signs, and are of aid in interpreting the often obscure underlying pathological processes.

A number of cases in which involvement of the diaphragm was of considerable aid in the eventual diagnosis have come under my observation during the past year. It is the purpose of this paper to briefly review the present-day ideas as to the action of the diaphragm in diseased conditions of the surrounding organs, and to illustrate the importance of some of the resulting physical signs by reports of the cases in which these signs appeared.

Conditions which involve the diaphragm may be broadly divided into two classes: (1) those which through irritation or inflammation of the pleural or peritoneal covering of the diaphragm give rise to a chain of symptoms which depend on the innervation of the diaphragm for their genesis, and (2) those which are caused by changes in the position of the diaphragm, which place the diaphragm at a greater or less mechanical advantage to perform its function.

The pleural and peritoneal coverings of the diaphragm are supplied by the phrenic nerves and the sixth to twelfth intercostal nerves. The outer rim, a space about three inches broad, is supplied by the lower intercostal nerves, while the remaining central portion is innervated by the phrenic nerves.

It has long been known that irritation of the pleural covering of the diaphragm often results in pain and tenderness over the phrenic nerves in the neck, and that this irritation is occasionally accompanied by tender points in the hypochondria. De Mussy[2] was the first to describe these points of tenderness, and they are still referred to as "De Mussy's buttons." Pain or tenderness in the immediate region of the diaphragm has not been noted in such cases. This would suggest that the pleural or peritoneal surfaces of the diaphragm when irritated give rise to pain referred along their nerves to the surface, after the manner of the viscero-sensory reflexes described by Head[3] and MacKenzie.[4] This is further substantiated by observations of MacKenzie[5] and Capps[6], who showed that irritation of the pleural surface of the diaphragm caused no local sensation of pain in the structure.

In 1911 Capps[7] reported a series of ingenious observations on the distribution of the pain sensation which occurred when the pleural surface of the diaphragm was irritated. In a number of cases of pleurisy with effusion, which required paracentesis, Capps inserted

[2] Archiv. Gén. de Méd., Paris, 1853, ii, 271.
[3] Brain, 1893, xvi, 1; ibid., 1894, xvii, 339; ibid., 1896, xix, 153.
[4] Symptoms and Their Interpretation, 1913, p. 71.
[5] Ibid., p. 215.
[6] Archiv. Int. Med., 1911, viii, 717.
[7] Loc. cit.

a long, blunt wire through the needle before any fluid had been drawn off. In this way he was able to make pressure on different parts of the diaphragmatic pleura and to observe the distribution of the painful sensations which resulted from this procedure. He found that pressure over the surface of the diaphragm caused painful sensations in areas remote from the point of irritation. He further found that these painful areas bore a constant relation to the portion of the diaphragm on which pressure was exerted. When pressure was made on the outer edge of the diaphragm there resulted a sensation of pain in the abdomen, in the flank, or in the lower thorax. On the other hand, when the central portion of the diaphragm was irritated, pain appeared along the ridge of the trapezius muscle or in the shoulder. These painful areas were frequently associated with hyperesthesia or hyperalgesia of the skin and with tenderness on pressure over these points.

The following cases will serve to illustrate the symptoms which occur with irritation of the pleural covering of the diaphragm:

CASE I.—H. C., male, aged forty-four years, was admitted to the Cleveland City Hospital on November 27, 1912. His family and past history were not important. On the day previous to admission he was seized with a sharp pain in the abdomen. The pain was most marked in the left upper quadrant, but was general over the left side of the abdomen, and was referred to the left flank as well. He vomited once; there was no blood in the vomitus.

When seen the patient was evidently in considerable pain. The heart and lungs were not remarkable, except that there were a few coarse, dry rales throughout both lungs. The excursion at both bases was good and there was a Litten's sign on each side. Deep inspiration seemed to increase the abdominal pain somewhat. There was tenderness over the whole left side of the abdomen, which was more marked in the upper quadrant, at which point there was slight spasm of the muscles on pressure. The temperature was 100° F. The respirations were 22 per minute. The pulse was 70. The urine showed no abnormalities. The white-blood cell count was 28,000.

On the day after admission the patient began to hiccough. The abdominal pain was still severe and the pain in the left flank persisted. The hiccough naturally suggested irritation of the phrenic nerve, but, on account of the distribution of the symptoms, it was deemed probable that the cause of the trouble lay beneath the diaphragm.

On the third day after admission it was noted that in addition to the tenderness there were definite hyperesthesia and hyperalgesia over the left upper quadrant of the abdomen. The patient continued to hiccough constantly. No further signs could be detected in the lungs. During the next two days the hiccough continued, though the abdominal pain entirely abated.

Six days after admission it was noted that pressure over the left phrenic nerve in the neck caused great pain, and that pinching the skin over the ridge of the left trapezius muscle also was very painful. There was no skin hyperesthesia. On this day the temperature, which had ranged between 100° and 102° F., since admission, became normal. The leukocyte count was 7500.

The pain and tenderness in the neck remained for twenty-four hours and then disappeared. The patient continued to hiccough almost constantly until the ninth day of his stay in the hospital.

On the tenth day the temperature rose again to 101.5° F., and the patient complained of pain in the right side of the abdomen, which was accompanied with tenderness in the right upper quadrant. There was also tenderness over the right phrenic nerve in the neck. The white-blood cell count was 16,000.

On the eleventh day a circumscribed friction rub was heard at the right base posteriorly. From then on the symptoms abated and the patient made a rapid recovery.

In this case the onset and early course of the condition strongly suggested an acute abdominal process. The development of uncontrollable hiccough pointed to irritation of the diaphragm, but at first the presumption was that the inflammation was below the diaphragm rather than above it, especially in the absence of any evidence of lung involvement. The appearance of the pain and tenderness over the phrenic nerve in the neck, along with the pain and tenderness and hyperalgesia of the skin over the ridge of the left trapezius muscle, pointed to an irritation of the central portion of the diaphragm. Irritation of the outer rim of the diaphragm, causing painful sensations in the lower dorsal segments, could account for the pain and tenderness in the left hypochondrium. The diagnosis was amply substantiated, it seems to me, by the appearance of a similar though not so well-marked chain of symptoms on the right side, accompanied as they were by a friction rub. It is especially interesting that at no time were there any signs even remotely suggesting the presence of a pulmonary infiltration.

CASE II.—E. R., female, aged twenty-two years, was admitted to the Cleveland City Hospital on November 20, 1913. She complained of vomiting and abdominal pain. The patient was in the third month of pregnancy. A few days before admission to the hospital she began to have pain on the right side of the abdomen, had been feverish, and had begun to cough. Physical examination showed a well-developed and nourished young woman. There was slight dulness at the base of the right lung, below the angle of the scapula. The excursion of the lung was somewhat limited on the right. The fremitus was slightly increased at the right base. There were a number of fine crackling rales over the right lower lobe posteriorly, with a somewhat prolonged expiration. The subcostal angle moved normally.

The abdomen was soft everywhere. There was no rigidity and no masses were palpable. The right upper quadrant was uniformly tender on pressure, and the skin of this region showed marked hyperesthesia and hyperalgesia. Examination of the cardiovascular system showed nothing abnormal.

The ridge of the right trapezius muscle was very tender, and the skin over this area was distinctly hyperesthetic. The patient hiccoughed frequently during the examination.

The temperature was 100° F. The respirations were 26. The pulse was 110. The urine was negative. The leukocyte count was 19,600.

Further observation on this case was not possible, as she left the hospital against advice, with the condition practically unchanged.

In this case the physical signs indicated an involvement of the lower lobe of the right lung. In the presence of abdominal pain, tenderness, and hyperesthesia of the skin, as well as of pain and of tenderness along the ridge of the right trapezius muscle, it is reasonable to suppose that an inflammation of the diaphragmatic pleura existed.

In the light of the above cases Capps'[8] observations on 19 cases of diaphragmatic pleurisy are of interest. Out of 19 cases he found that 8 had pain in the abdomen as far down as the navel, and that in 11 cases the pain extended all over one-half of the abdomen. The pain was spontaneous, but was associated with tenderness on pressure. It has been my experience in such cases that the tenderness on pressure over the abdomen is due to cutaneous hyperesthesia. In 11 out of the 19 cases he found pain over the ridge of the trapezius muscle or on the side of the neck, usually associated with hyperesthesia of the skin.

In these cases of inflammation of the diaphragmatic pleura the distribution of pain is either along the phrenic nerve, and is made evident in the third and fourth cervical segments, or along the sixth to twelfth intercostal nerves, with a distribution in the lower dorsal segments, substantiating the view that the pain sensations resulting from irritation of the serous covering of the diaphragm is a true viscero-sensory reflex.

In order to understand the effect of change of position of the diaphragm a brief review of its actions is necessary. During inspiration the contraction of the diaphragm increases the vertical diameter of the thorax. The diaphragm descends a certain distance and withdraws from the chest walls in the regions of the pulmonary sinuses allowing the inflated lungs to descend. The older conception that the diaphragm forces the organs immediately below it downward, with a piston-like motion, is probably not tenable at

[8] Loc. cit.

present. The scalene muscles and the intercostals lift the ribs during inspiration which action results in drawing the costal borders away from the median line, or in other words, in a widening of the subcostal angle. The contraction of the diaphragm, besides increasing the vertical diameter of the thorax, will also tend toward an inward pull along its line of attachment especially along the anterior and lateral insertions which will be in direct antagonism to the outward flaring of the subcostal angle, caused by the action of the scalene and intercostal muscles.

Hoover[9] has demonstrated the presence of this antagonism very conclusively. When the diaphragm of a dog was stimulated with a strong electric current, causing a marked contraction, the subcostal angle was seen to be drawn sharply toward the median line. On the other hand, when the roots of the phrenic nerves on both sides were cut, resulting in complete paralysis of the diaphragm, the inspiratory flaring of the subcostal angle was very much increased over the normal.

Now if for any reason the diaphragm assumes a lower position than normal, especially in its anterior portion, the pull of its inspiratory contraction will be exerted more directly on its points of insertion, which will place the diaphragm at a greater mechanical advantage and will give it the power to equalize or overcome the outward pull of the scalenes and intercostals. This will result in an abolition of the normal flaring of the subcostal angle, or in an actual narrowing of the angle with a movement toward the median line instead of away from it. On the other hand, conditions which displace the diaphragm upward will accentuate the normal upward curve of the diaphragm, with a resulting diminution in its ability to pull against the muscles which raise the thorax and cause the normal outward movement of the subcostal angle.

Hoover[10] has shown experimentally that changes in position of the diaphragm will have these effects on its pulling power, and he has further shown that in certain diseased conditions which alter the position of the diaphragm in an upward or downward direction the movements of the subcostal angle may be of distinct diagnostic assistance.

While very marked retractions of the subcostal angle on inspiration may be plainly visible, it is often impossible to determine whether the retraction is present without the use of palpation. The best method of palpation is to place the thumbs along the line of the costal margin, pointing toward the ensiform cartilage, and have the patient breathe deeply. Slight limitations of motion or slight retractions of the angle are then readily appreciated. This is especially necessary in fat persons, or in persons in whom the respiratory movements are generally diminished.

[9] Archiv. Int. Med., 1913, xii, 214. [10] Loc. cit.

I have observed a number of cases in which the position of the diaphragm affected the movements, some of the more interesting of which I wish to discuss:

CASE I.—S. A., male, entered the hospital with a low-grade infiltration of the base of the right lung. He had a chronic nephritis with some edema of the extremities. His heart was not remarkable at admission, but in a few days the area of cardiac dulness began to increase to the left and right. The heart sounds became more distant daily. There was no blunting of the cardiohepatic angle, and no change in dulness or change of position. There was no paradoxical pulse. On inspiration the costal margin on the left definitely approached the median line, while that on the right swung out in the usual manner. The left lung and pleural cavity were clear. During the next twenty-four hours the cardiac dulness continued to extend to left and to right. The left border of cardiac dulness reached nearly to the anterior axillary line. The retraction on the left became more marked as the cardiac dulness increased. An exploratory puncture of the pericardium showed the presence of a clear, straw-colored fluid in the pericardial sac and some 100 c.c. of fluid were removed. On the removal of the fluid the area of cardiac dulness returned to normal and the retraction of the costal margin disappeared.

The pericardium filled up again twice with a repetition of the same signs, which disappeared at once after the fluid in the pericardium was removed again.

CASE II.—R. N., was admitted to the hospital suffering from severe myocardial decompensation, with edema of the legs, enlarged and tender liver, shortness of breath, and orthopnea. The heart's action was weak and irregular, and there was considerable enlargement of the cardiac dulness both to left and to right. There was no retraction of the subcostal angle. Under rest and digitalis the symptoms rapidly abated, the edema left his legs, and the heart dulness returned almost to the normal size. The pulse slowed and became regular. During a routine examination of the heart a few days later it was found that the cardiac dulness had again increased in size, especially to the left, and that there was apparently a distinct blunting of the cardiohepatic angle. It was noted that there was now a distinct retraction of the left costal margin. Both chest cavities were clear. The patient was perfectly comfortable and lay flat in bed. The cardiac dulness continued to increase in size and the retraction of the left costal margin to become more marked. Roentgen-ray picture taken at this time showed a large pear-shaped shadow of the heart area, which was much denser than the usual cardiac shadow. After a few days the above-mentioned signs began slowly to retreat. The dulness became less in size until it reached the normal, and the retraction coincidentally became less until it disappeared entirely, giving place to a normal movement

of the subcostal angle. A Roentgen-ray picture taken at this time showed a heart normal in size, the difference in the two pictures being very striking. In the absence of any signs of cardiac embarrassment, taken with the rapid change in the signs, also with the rapid diminution in the size of the heart shadow, it is reasonable to suppose that we were dealing with an effusion into the pericardium, though no exploratory puncture was made.

In these two cases the pericardial sac was filled with fluid. The weight of this fluid depressed the diaphragm on the left side, especially in its anterior portion, bringing that part of the diaphragm lower and giving it a greater mechanical advantage, which resulted in a pull strong enough to overcome the intercostals and scalenes, and therefore caused a retraction of the subcostal angle on the left.

I have observed several cases of cardiac decompensation with great enlargement of the right heart, wherein there has been slight retraction of the left costal margin. The effect on the diaphragm of the enlarged right heart will be the same as that of an overfilled pericardium, but to a less degree. In my experience the retractions occurring with dilatation of the right heart are never so marked nor so constant as in the two cases of pericardial effusion cited above.

In pneumothorax and in pleurisy with effusion where there are no adhesions the depression of the diaphragm will result in retraction of the subcostal angle. In two cases of pneumothorax the retraction has been very definite. It has been present in practically all cases of fresh pleurisy with effusion which I have seen in the last twelve months at the Cleveland City Hospital, even when the effusions were small in amount.

Fluid may, when encapsulated by adhesions, however, be present in a considerable amount without the presence of a retraction of a subcostal angle. The following case illustrates this point:

Case III.—R. B., two days before admission to hospital, had had sharp pain in the right side of the chest, accompanied by chill. On admission, examination of the lungs revealed slight dulness in the right axilla with a few crackles and slight tubular breathing. There was decided tenderness over the skin along the ridge of the right trapezius and over the right phrenic nerve in the neck, and also tenderness and hyperesthesia of the skin in the right hypochondrium. Slowly signs of fluid appeared at the right base posteriorly, which continued to increase. The anterior border of the flatness extended only to the midaxillary line. Examination of the anterior portion of the chest showed no signs of fluid. There was no retraction of the right costal margin, though signs of fluid continued to increase posteriorly. On tapping a pint of fluid was removed.

In this case the signs of fluid were confined to the posterior portion of the chest, and the history and the signs on admission suggest the presence of an acute fibrinous pleurisy of the diaphragm and parietal pleura. Probably on account of this the fluid was held

in a limited portion of the pleural cavity and therefore could not get forward far enough to depress the anterior portion of the diaphragm. This would explain the absence of retraction of the subcostal angle in this case, even though there was a considerable accumulation of fluid in the pleural cavity.

Certain cases of old adhesive pleuritis will show a marked retraction of the costal margin on the affected side during inspiration. I have observed several such cases. It is presumable that in this condition the pleural sinus is obliterated and that the diaphragm acquired what amounts to a much higher attachment than normal. In these cases the pull of the diaphragm when it contracts will be more direct, and will, therefore, be more powerful than normal, and will result in a retraction of the costal margin.

In contradistinction to the above class of cases are those in which the diaphragm is pushed up from below so that the pull of its contraction is less than usual. This will increase the advantage of the scalene and intercostal muscles, and will result in an increased outward movement of the subcostal angle. This is frequently seen in enlargements of the liver or spleen, but is probably most important in large collections of fluid below the diaphragm. In large subdiaphragmatic abscesses the signs often simulate those of fluid within the pleural cavity, except that there will be an increased flaring of the costal margin on the affected side on account of the accumulation of pus below the diaphragm. Hoover[11] reports two cases in which the differential diagnosis between empyema and subdiaphragmatic abscess rested entirely on the increased outward movement of the subcostal angle. Subsequent operation in both cases proved the diagnosis to have been correct.

SUMMARY. 1. Inflammation or irritation of the pleural or peritoneal surface of the diaphragm does not give rise to local symptoms. The pain resulting from such processes is referred upward along the phrenic nerves to the third or fourth cervical segments or downward along the sixth to twelfth intercostals into the lower dorsal segments. The pain is usually accompanied by tenderness and hyperesthesia or hyperalgesia of the skin. The recognition and interpretation of these signs may be of considerable importance in differential diagnosis between intrathoracic or intraperitoneal disease, in the absence of any signs in the lungs.

2. When the part or the whole of the diaphragm is forced downward the contraction of the diaphragm exerts a more powerful inward pull along the line of its attachments. This is especially marked when the anterior portion of the diaphragm is depressed. This will result in a lessening of the outward excursion of the subcostal angle, or an actual retraction along the line of diaphragmatic attachment. Conversely any condition which lifts the diaphragm upward lessens the strength of the inward pull of the contracting

[11] Loc. cit.

diaphragm, with the result that the normal outward movement of the costal margins will be increased.

3. The presence of a retraction or of an abnormal outward flaring of the subcostal angle will often be of aid in the explanation of obscure diseases of the viscera which lie immediately above or immediately below the diaphragm, especially in pericardial effusion or in subphrenic abscess.

PLEURISY.

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Pleurisy in one of its many forms is the commonest of the diseases of the chest, and the most unmanageable. It is often less easy of successful treatment than pneumonia, and sometimes leaves behind it more permanent mischief. Slight attacks may occur without being recognized, explaining the frequency of pleuritic adhesions found in the postmortem examinations of persons who were never known to have been ill. It occurs at all ages, from early infancy to advancing years, but is more frequent in the male between youth and middle age. Its etiological data, bacterial or general, are not, in our present knowledge, quite well enough understood to establish a definite classification. The disease is usually one-sided, preferably confined to the right, though occasionally it is bilateral, and then is apt to be secondary to phthisis or septicemia. It is primary or secondary. By the term primary is meant inflammation of the pleura in a time of health, being mainly limited to the membrane itself, with secondary constitutional results of fever, or if exudation be present, to the mechanical effects of pressure in addition. Secondary pleurisies are by far the more common and the more serious, associated as they so often are with disease of the lungs or neighboring viscera, and sometimes complicating infective processes in the body.

Pleurisies are also divided into the acute and chronic, based upon clinical symptoms, often found, however, to be of doubtful significance. The chronic is frequently of that form from the onset, but it is more likely to be consecutive to the acute. The chief varieties of pleurisy are the fibrinous, the serofibrinous, and the purulent. The predominant causative bacteria are the tubercle bacilli, the pneumococci, and the streptococci. The exudates are often found to be sterile and when a purulent exudate is sterile it is invariably tuberculous. Bacilli of lesser importance exist in the mixed forms.

Fibrinous or plastic pleurisy is often confined to a circumscribed area, lasting for a few days and terminating by adhesions. Its

friction sound is not propagated, but dies where it was born and may readily escape detection. Diffused spots of subacute inflammation not uncommonly occur in connection with chronic nephritis, and if there be friction in the cardiac region it may be influenced by the rhythm of the heart as well as by respiration.

Chronic dry pleurisy, which is usually tuberculous, has in many instances an acute onset, causing thickening of the pleura, extensive adhesions, and fibrosis of cortical portions of the lung. It may remain localized for months or even for years, finally proving fatal from pulmonary phthisis or from acute miliary tuberculosis. I have known of a case of extensive plastic pleurisy of many years' duration to terminate fatally from pneumothorax. The autopsy revealed extensive adhesions binding the lung posteriorly from base to apex. The non-adherent portions of the lung were compressed backward by accumulated air from a ruptured tuberculous ulcer. The pleural cavity was practically free from liquid.

Acute fibroserous pleurisy attacking one in apparent good health after exposure to cold or possibly to traumatism begins with a chill or usually a sense of chilliness, stabbing pain in the chest, disturbed breathing, and fever. A pronounced chill occurs less frequently in pleurisy than in pneumonia, algid attacks taking the place of the former at irregular intervals during the first few days. Pain, on the contrary, is usually intense in pleurisy. It is lancinating, as if from the thrust of a sharp instrument, and often makes the patient cry out on taking a deep breath or after a cough. It is also increased by pressure and by movements of the body.

The pain lessens or ceases altogether when adhesions occur, or when the inflamed surfaces of the pleura are separated by liquid effusion, though it may return intermittingly during the patient's illness from exacerbations of the original attack. The seat of election of pleuritic pain is a few fingers' breadth below the nipple, though its point of maximum intensity may be elsewhere in the lateral region of the chest or posteriorly below the inferior angle of the scapula. Occasionally the pain is referred to the lower dorsal region or to some part of the abdomen, giving rise, in the absence of careful examination of the chest, to grave errors in diagnosis. I have known of two patients suffering from pain in the abdomen, one a girl of five years, the other a man about forty years, to be operated upon, the one for appendicitis, the other for perforated gastric ulcer. Both cases ended fatally, showing at the autopsy double serofibrinous pleurisy in the child, and localized diaphragmatic pleurisy in the man. The different seats of pain do not throw clear light upon the precise localization of the disease or its extent, but merely indicate the side affected. Sometimes, however, the pain of circumscribed pleurisy corresponds exactly with the seat of inflammation. In double pleurisy, pain is often felt on one side alone or it may be confined to the middle of the thorax. It is rarely itself

double, but may change from one side to the other, according to the progress of the disease, each one of the pleuræ being successively involved.

The respirations at first are always embarrassed and painful in consequence of efforts at full breathing, the inspiration being cut short before it is completed. But there is not true dyspnea until the lung is compressed by effusion, and perhaps not then unless it be rapid and copious. Cough is sometimes wanting, but in the majority of cases the patient has a short, dry, shallow cough with attempts at restraint, because of the pain to which it gives rise. It is occasionally attended with scanty expectoration of thin, frothy mucus, but if it be abundant and opaque, an association with bronchitis or other affection of the lung is found to exist. In recent cases of moderate severity the pulse bears a close relation to the height of the fever, and is not greatly in excess of the normal. In cases of large effusion with sudden compression of the lung there is a disturbed balance between the pulmonary and general circulation, sufficient blood not passing from the right ventricle into the lungs, and through them to the left side of the heart and the arterial system. Under these circumstances the action of the heart is violent and the pulse at the wrist is frequent and repressed to such a degree as to cause danger from suffocation.

A young man under my care, laboring under an acute pleuritic attack with large effusion, left his bed in the absence of the nurse and walked some distance to the end of the room, the exertion proving almost fatal. On his return to bed the patient was gasping for breath, his heart was beating violently, and his pulse was indicative of lowered arterial tension. Venesection was followed by prompt relief to the threatening symptoms.

The fever of acute pleurisy is of remittent type, with exacerbations toward evening, lasting until the exudate reaches its maximum, when it gradually declines without an attempt on the part of nature to promote a crisis. In some cases the fever returns at irregular intervals, but it finally drops to the normal. Should the temperature be persistently elevated and intermittent there is every reason to suspect the existence of pus in the pleural cavity.

The decubitus of the patient suffering from pleurisy is frequently changed during the course of the malady. At the onset, when there is pain and tenderness on pressure, while the patient avoids lying directly on the affected side, his body is often inclined in that direction. Late in the disease he assumes the dorsal decubitus, but when the effusion is very great the patient naturally prefers lying on the diseased side to relieve the healthy lung of the weight of the fluid. The duration of the active symptoms of acute primary pleurisy with moderate effusion is from ten to twenty days, when absorption begins progressing slowly, however, before the process is completed, often lasting for many weeks. Retraction of portions of the

chest, impairment of resonance, and feebleness of breath sounds with coarse friction may exist for an indefinite length of time, the patient being able to walk about, though looking ill and suffering from dyspnea on exertion.

Chronic pleurisy, as a rule, is the continuation of the acute, though it may result from some low-grade infection from the beginning, in which case the greater number are secondary to a constitutional malady or to some visceral disease. The affection sometimes exists in the form of what is termed latent pleurisy, without any of the general symptoms, unless dyspnea be present, and yet one side of the chest is found to be largely filled with fluid. The physical signs alone reveal the disease, and in every case of suspected infection of the chest a careful examination should always be made.

The following case is mentioned to show how a person laboring under pleurisy of chronic form with enormous effusion was able to perform the full duties of his position without much inconvenience:

C. L., a Chinaman by birth, and cook in a private family, aged sixty-six years, was admitted into the Bryn Mawr Hospital on April 1, 1914. He had been troubled with cough, slight pain in the right side, and shortness of breath for about four weeks, but did not give up work until the day of his admission. On examination the right side of his chest was found to be distended, and there was scarcely any perceptible movement during respiration. There was flatness on percussion and absence of vocal vibrations from three inches below the clavicle in front and below the spine of the scapula posteriorly. At the apex of the lung front and back the percussion note was high-pitched and tympanitic. The breath sounds were altogether absent in the dull regions. Above the level of the fluid posteriorly, and near the spinal column over the compressed lung, there was bronchial respiration and bronchophony. The heart was not much displaced. On April 3, the effusion was so great that the whole of the right side of the chest was absolutely dull on percussion, and breath sounds were everywhere absent except at the root of the lung. Aspiration of the chest was performed, with the result of removing 2200 c.c. of serous fluid, afterward found to be sterile. The patient left the hospital April 23 much improved in health, but suffered a relapse and was readmitted on May 3. The right chest had already undergone retraction. There was dulness posteriorly below the angle of the scapula, and the breath sounds were harsh and distant. Elsewhere on the right side there was tympanitic dulness on percussion and an approach to bronchial breathing. On July 3 the patient was discharged for the second time, with the view of being sent to a sanitarium for outdoor treatment.

Two boys under my care were also cases of latent pleurisy, the first, aged ten years, had passed a section of tape-worm shortly before my visit, and I found him in bed suffering from abdominal

pain, naturally attributed to the irritation of the parasite. There was an absence of symptoms referable to the chest except slight dyspnea, which led me to discover that the patient's left pleural cavity was more than half filled with fluid. The second boy, aged five years, was brought to the country to recover from a gastric attack. He had slight fever, epigastric tenderness, nausea, and vomiting. On examining his chest I found a large effusion on the right side, with all of the characteristic physical signs of pleural inflammation. Both of these patients made good recoveries.

A remarkable instance of pleurisy without marked symptoms was that of Mrs. R., aged forty-five years, who when I first saw her was up and about attending to her household affairs. I was informed that she had been indisposed for a week or more, that she had occasional cough but without pain, and was feverish at night. Examination of the chest revealed dulness on percussion, with absence of breath sounds and of vocal fremitus over the whole of the right lung. There was entire absence of movement of the right side of the chest during respiration, the intercostal spaces were bulging, and the adjacent organs displaced. I left the patient's house to arrange for immediate tapping of the chest, and before I had time to return a message was received that sudden death had occurred after the patient's exertion of going up stairs to the second floor.

The modern practice of early thoracentesis has notably lessened sudden death in pleurisy, though it is still occasionally reported. I once knew fatal syncope to occur, at the Bryn Mawr Hospital, during operation for the removal of fluid from the chest of a robust colored man suffering from acute pleurisy. An autopsy was not allowed.

In cases of pleurisy of long standing neglect the chest is sometimes enormously distended and the comparative immobility between the two sides is most remarkable, the patient raising up the sound side while that of the seat of disease is almost quiet. The intercostal spaces are widened, effaced, and sometimes bulging. The nipple is abnormally distant from the central line of the sternum, and I have often observed it elevated. The neighboring viscera are displaced, chief among them being the heart, which is carried far to the opposite side of the chest. After absorption of the fluid or when it has been mechanically removed, atmospheric pressure is found to have pushed in the parietes of the chest toward the unexpanded lung, giving rise to contraction not only in circumference but from above downward, displacing the scapula and obliterating the intercostal spaces by encroachment of the ribs. The shoulder droops and the body inclines to the affected side, giving the patient a peculiar "lob-sided" gait. In a right-sided pleurisy under these circumstances the liver is drawn up and the heart sometimes pulled over to the right, quite the reverse of what happens when effusion exists.

In a chronic pleuritic case coming under earlier observation the lung, though pushed upward toward the mediastinum or spinal fossa, is less adherent and reëxpands more fully when absorption of the fluid takes place, or is withdrawn by aspiration, and therefore retraction of the chest is less marked. Purulent pleurisy occasionally follows injury to the chest with deep-seated lacerations or it is not infrequently secondary to an acute infective disease. Puerperal pleurisy is often purulent, bilateral, and consequently fatal. Primary suppurative pleurisy is extremely rare in the adult. It is almost always serofibrinous at first, becoming purulent during its subsequent course. It is a common disease of infancy and childhood, and in many instances at that period of life it is purulent from the beginning. The general symptoms are not in any particular different from those of serous pleurisy, with the exception of the persistence of fever and its marked evening rise. Before the days of antisepsis there were many errors of diagnosis and a high mortality of empyema, but now exploratory puncture leads to prompt recognition of the disease and immediate operation. Formerly attempts of nature at spontaneous cure were met with by the discharge of pus through a perforated bronchus or by the formation of a subcutaneous abscess in the parietes of the chest communicating with the pleura, *pleuritis necessitatis*.

In 1886 Miss S., aged eighteen years, was under my care, suffering from acute serous pleurisy. On my first visit there was unmistakable evidence of left-sided pleurisy. Effusion took place rapidly and was copious. In the second week two pints of semi-opaque fluid were removed from the pleural cavity by aspiration. Cough was excessively annoying, and was continuously troublesome until the beginning of the fourth week, when after a violent paroxysm the patient expectorated a large quantity of extremely fetid pus. The discharge was brought up after cough, and on changes of position for many weeks. The patient became profoundly hectic and greatly emaciated, but after a prolonged illness recovered. She is now living and in good health.

Another incident of empyema is perforation of the diaphragm and the escape of pus into the peritoneal cavity, causing local or general inflammation. I have known of two such cases, both terminating fatally after operation. One, a young lady, the subject of tuberculous pleurisy of acute onset, with a copious effusion lasting for many weeks before the fluid was appreciably absorbed. In course of time her general health was sufficiently improved to enable her to go to the far west in search of a suitable climate, which was successfully accomplished, with good results. A second attack of pleurisy, however, was soon followed by suppuration, and pus discharged through the diaphragm, causing a walled-off abscess in the right hypochondrium.

My second patient, a saloon-keeper living in the West, aged forty

years, was attacked with right-sided pleurisy, the effusion becoming rapidly purulent, perforating the diaphragm, and causing general peritonitis. The disease was far advanced when the patient came under observation, and being an extreme alcoholic, he developed septicemia and died soon after being operated upon.

An incident of extension of infection from below upward was that of John C., aged fifty years, admitted into the Bryn Mawr Hospital on June 23, 1914, having a subphrenic abscess associated with pyopneumothorax, caused by perforation of the diaphragm, establishing a communication between the subdiaphragmatic region and the right pleura. The symptoms were abdominal and thoracic, the former more especially, as shown by a large, painful area of resistance in the hypochondrium. The thoracic symptoms were high-pitched tympanitic resonance over the lower half of the right chest, restriction of movement during respiration, with muffled bronchial and occasionally amphoric breathing posteriorly below the angle of the scapula. The normal liver dulness was replaced by tympanitic resonance on percussion. Under local anesthesia a free vertical incision was made in the right hypochondrium, giving exit to a large quantity of extremely fetid pus containing gas. A counter-opening was made in the dependent part of the abscess to insure free drainage. Several weeks later the chest was opened in the anterior axillary line and the sixth rib resected. The patient recovered and left the hospital on November 23, 1914.

A rare case of pleuritis acutissima of foudroyant type, rapidly becoming empyemic, was recently under my observation at the Bryn Mawr Hospital. Ross P., aged thirty-four years, a teamster, of intemperate habits, was admitted into the Hospital on December 12, 1914. The history he gave was that he took cold from exposure in a rain storm, and was confined to the house for one week before coming to the hospital with a troublesome cough, extreme malaise, and finally a chill and pain in the left side. He was complaining on admission of sharp pain in the left side and difficulty in breathing. He had a high temperature, frequent pulse, and excessive cough, with mucous blood-stained expectoration. The tongue, dryish and brown, was tremulously protruded. He was incoherently delirious, and was inclined to get out of bed. There was dulness on percussion over the lower half of the left lung posteriorly, with absent vocal fremitus, feeble breath sounds, much prolonged expiration, and distinct egophony below the angle of the scapula. On December 13 the patient become violently delirious and jumped out of the window, falling on the ground, a distance of twelve feet, but without sustaining serious injury. The patient's delirium lasted for a week or more with fever going at one time to 105°, and on December 25, on exploratory puncture, the effusion was found to contain pus. Owing to the patient's excitable condition, operation upon the chest was delayed until January 5, 1915, when 600 c.c.

of purulent fluid were evacuated from the chest by incision and resection of one rib. The infection was found to be pneumococcic. The patient is now, January 14 recovering.

Prominent among other varieties of pleurisy depending for the most part upon anatomical conditions are the diaphragmatic, hemorrhagic, interlobar, and the pleuropneumonic.

In restricted pleurisy when the diaphragm is the exclusive seat of the disease the general symptoms are to be mainly relied upon in making a diagnosis. The physical signs are indefinite and often altogether absent. Auscultation sometimes reveals feebleness of the vesicular murmur and a few subcrepitant rales at the base of the lung of the side affected. The attack begins suddenly, preceded by a chill and followed by high fever, violent pain, and excessive dyspnea. The pain is usually referred to the hypochondrium, extending to the epigastrium, and sometimes to the ileolumbar region of the corresponding side. It is increased by deep inspiration, and is made intolerable by hiccough and vomiting. The painful regions are very tender to the lightest touch. This is especially true, as has been pointed out by M. Gueneau de Mussy, of a spot one or two finger's breath from the linia alba on the level with the bony part of the tenth rib. When this point is even slightly pressed upon the patient cries out, and there is also a sudden increase of dyspnea, seeming to threaten suffocation. This spot M. de Mussy called "le bouton diaphragmatique." The phenomenon is explained by a hypersensitive branch of the phrenic nerve. Pressing upon the hypochondrium from below upward also gives rise to great pain. The respirations are excessively frequent and almost convulsive in character. The patient breathes with the ribs rather than with the diaphragm. The difficulty of breathing is sometimes so great as to cause orthopnea, the patient leaning forward and supporting the painful part with the hand to immobilize the chest.

Hemorrhagic pleurisy is of rare occurrence in the primary form. In the majority of instances it is secondary to some organic disease or to a general infection. Its physical signs do not differ practically from those of the serofibrinous variety, and accurate information is only to be obtained by exploratory puncture.

Some years ago a man of middle age, who was under my care suffering from an acute exacerbation of chronic articular gout, was taken with pain in the right side, with rapid filling up of the pleural cavity. He had enlargement of the heart, with long-standing valvular disease and cirrhotic kidneys. On being tapped the pleural effusion was found to be hemorrhagic. Death occurred after a short illness from uremia.

Another patient under my care was a lad, aged eighteen years, of good previous health and about to enter college, who took ill with pyrexia which proved to be typhoid of irregular type. At the beginning of convalescence he was attacked with left-sided pleurisy,

followed by a rapid and copious hemorrhagic effusion. The patient after an illness of many weeks finally recovered sufficiently well to get about and retained improved health until several months later, when he was taken suddenly ill with tuberculous meningitis, ending fatally in about ten days.

Interlobar pleurisy with sacculated effusion, serous or purulent, is always difficult to diagnose, and often impossible to locate. It rarely exists alone, but is associated with extensive fibrinous or serofibrinous inflammation. A cystic empyema is the more common, and is sometimes an infection associated with pneumonia. Persistent fever, with increasing evening exacerbations and a high leukocyte count, leads to exploratory puncture, and if purulent fluid be found, operation is called for.

A colored woman, by occupation a cook, under my care a few years ago, was taken ill with pneumonia of the apex of the right lung, beginning with a violent chill and followed by fever, dyspnea, and cough, with rusty sputum, a pseudocrisis occurring on the ninth day of the patient's illness. The fever increased again with marked evening rise, lasting for many weeks. The leukocyte count varied from 17,000 to 24,000. The cough was most annoying, and the expectoration, scanty at first, increased in quantity and became purulent. Repeated exploratory punctures failed to reveal the presence of pus. The physical signs were localized dulness and rough breathing near the original seat of pneumonia, and impairment of resonance from the spine of the scapula to the base of the lung, with coarse friction and bronchovesicular respiration. After an exhausting illness of many months the patient was able to resume her former occupation. The case unquestionably was one of empyema in the fissure between the upper and middle lobe of the right lung, remaining undiscovered by puncture, and finally discharging through a bronchial fistula. Pleurisy and pneumonia are often combined; indeed, pneumonia rarely exists without some degree of plastic inflammation of the pulmonary pleura; but to properly constitute a case of pleuropneumonia there must be a decided effusion. More than the ordinary amount of pain indicates the coexistence of the two diseases, and if there be positive flatness on percussion at the base of the lung, lessened or absent vocal fremitus, indistinctness of bronchial breathing and perhaps egophony, the diagnosis can be no longer in doubt. The convalescence is more apt to end by lysis, and is prolonged by fluid remaining to be absorbed.

The physical signs of pleurisy vary according to the stage of the disease and the amount of effusion in the pleural cavity. Compared with the general symptoms they are of greater importance in forming a correct diagnosis. The expansion of the lower part of the affected side is less than that of the sound side, even before effusion occurs, mainly in consequence of painful breathing, and the cor-

responding side of the chest is also somewhat retracted as may be shown by measurement.

Palpation is not only of use in determining the degree of lessening of the respiratory movements, but is also of great importance in estimating the strength of the vocal vibrations, which are absent in deep effusions and feebly present in others, a physical sign of much importance from a diagnostic point of view. Palpation is a useful means of determining the degree of displacement of the heart and the extent of downward displacement of abdominal organs. In pleurisy with large effusion on the right side the free edge of the liver is often felt below the costal border, and if the left side be the seat of disease, the outlines of the spleen are sometimes distinctly made out.

The sounds on percussion in pleurisy are the most important of all of the physical signs. At the onset there is no material change, but when effusion occurs it gives rise to dulness on light percussion, becoming gradually flat as the liquid increases in quantity.

Fluid dulness has a character of its own, if percussion be not too strong, being airless without resonance, and different from the dulness of lung-consolidation, not unlike the sound obtained on striking the thigh. The flatness is more decided at the lower portion of the chest and becomes gradually less from below upward. If the disease be left-sided, allowance must be made for the resonance of the stomach, which often modifies the sound as far up as the eighth interspace. As the effusion increases the upper line of dulness when the patient is sitting upright is not horizontal but assumes more or less the shape of an extended letter S, curving upward and forward to the axillary region, thence downward to the lower part of the sternum. The percussion note above the level of a large effusion is dull and tympanitic, and in front below the clavicle it has high-pitched tympanitic or Skodaic resonance of exaggerated intensity, contrasting strongly with the flatness lower down. The depth of the sound and its tympanitic quality is one of the most characteristic signs of pleuritic effusion, extending up as high as the third or fourth rib anteriorly. When the pleural cavity is quite filled with fluid the percussion note is dull everywhere on the side affected, except at the root of the lung, where the bronchial tubes are large and rigid. Under these circumstances, if the disease be on the left side dulness on percussion replaces the normal tympanitic resonance of Traube's semilunar space following depression of the diaphragm, and with it the stomach which lies in close contact. In rare cases of large left-sided effusions the lifting power of the lung may be sufficient to counterbalance the weight of the fluid to the extent of limiting the depression of the diaphragm and not greatly interfering with the tympanitic resonance of Traube's space throughout the attack.

The auscultatory signs of pleurisy vary greatly according to the

extent of the inflammation, the amount of effusion, the degree of compression of the lung, and the number of adhesions. The respiratory murmur, somewhat enfeebled at first by restricted movement of the lung from pain, is still more so when liquid effusion occurs. As the effusion takes place the breath sounds become more feeble and rough, with prolonged expiration, which in the lower part of the chest may be altogether absent. Above the level of the fluid, where the compressed lung, still containing air, is in contact with the walls of the chest or only separated by a small amount of liquid, the respiration becomes more or less bronchial, its intensity varying according to the degree of condensation of the lung, and the voice is bronchophonic. Bronchial respiration and bronchophony coexist in pleurisy, but the latter has a vibration or quivering in its tone which never exists, at least to the same degree, in pneumonia proper. When the bronchial respiration is not loud the resonance of the voice becomes less bronchial, but its vibration is increased and so-called egophony is heard.

The sound of egophony is not of much diagnostic importance in pleurisy, because it requires for its production a thin stratum of liquid intervening between the lung and the side of the chest, and therefore a moderate pressure upon the bronchial tubes. The sound ceases entirely when the effusion is large or else it is converted into bronchophony, of which it is merely a modification. The sound has been known to be propagated through a layer of false membrane after the pleural liquid has been withdrawn. It has been called one of the fancy signs of pleurisy. Its full though rare development once heard is never forgotten. The egophonic voice, when it exists, is best heard between the anterior axillary line and the scapula or in the interscapular region of the affected side. It is more frequently heard in women and children because of the higher pitch of their voice.

Another sign of pleurisy more important than the resonance of the voice and pathognomonic of the disease is the friction sound. It is heard both upon inspiration and expiration, more especially the former, and is often irregular from sticking together of the opposed pleural surfaces, which are released by an unusually deep inspiration such as that after cough. The friction sound is most liable to be confounded with a rhoncus, which is itself often perceptible to the touch; but a friction sound is seldom so loud as a rhoncus, and is rather increased by deep inspiration, whereas a rhoncus is altered or ceases after a vigorous cough. It is also characteristic of a friction sound that it is rendered more distinct when firm pressure by the stethoscope or by the ear is made against the chest. Friction occurs under two different circumstances; at the beginning before serum is effused and toward the termination of the disease when the liquid has undergone absorption or has been evacuated by tapping and the two inflamed surfaces of the pleura again come

in contact. At the close of the disease it is coarser and louder, and is best heard below the angle of the scapula or in the lateral region of the thorax. One reason why a friction is so often overlooked is because it is a sign rather than a sound, as shown by slight jerking movements of the chest. The character of friction sounds vary from the finest crepitation to the sole-leather friction or "bruit de cuir neuf" sometimes heard at a distance from the patient and often perceptible to the touch. Pleural crepitation occurs in volley form, resembling the crepitant rale of pneumonia, but it is finer, more moist, and is directly under the ear. I have occasionally found it in association with the sounds of catarrhal bronchitis, especially when the patient had violent fits of coughing.

The physical signs of pleurisy in infancy and childhood show great variations and cannot alone be depended upon, but must be compared with the general symptoms and the history of the attack in making a diagnosis. Of the diseases of the chest in children, pleurisy is the disease in which mistakes in diagnosis are most often made. Fibroserous and suppurative pleurisy both occur in early life, but the purulent form is relatively more common in infancy and not infrequently occurs *d'emblée*. The prevalence of the purulent disease in infancy is shown by the modern records of the Hospital for Sick Children. Dr. Henry K. Dillard informed me once that when he was resident physician at the Children's Hospital in Philadelphia there were five infants, varying in age from ten months to two years, operated upon for empyema in one winter. The operation in each case was by free incision and resection of one rib. The patients all recovered. In the Children's House of the Bryn Mawr Hospital there were eleven patients, mostly infants, operated upon for empyema within one year. The physical signs of pleurisy in children often resemble those of pneumonia, and it requires great care on the part of the physician to avoid a diagnostic error. The chief source of confusion is the persistence of bronchial breathing throughout the dull region of a large effusion, with entire absence of vocal fremitus. In different parts of the affected side of the chest the respirations may be intensely tubular. Friction sounds are rarely heard in young children, and the same may be said of feebleness of the breath sounds. Another difference is the comparative absence of visceral displacement, which is accounted for by the flexible chest of the child yielding readily to fluid accumulation, pressure not being expended upon the adjacent organs to the same extent at least as in the adult.

The diagnosis of pleurisy is readily made in most instances. An uncomplicated and well-characterized case cannot be confounded with any other affection. That is, when distention of the chest, absolute dulness on percussion, faintness or absence of vocal fremitus, feebleness or absence of respiratory murmur, and displacement of

viscera coincide with pain, irregular breathing, and fever. If the general symptoms be too much relied upon the diagnosis in many cases would be puzzling, but with the aid of the physical signs a satisfactory conclusion can be promptly reached. Pneumonia, with pleurisy is often confounded, but differs from the latter in the violence of its initial chill and the character of the pain, which in uncomplicated pneumonia is moderate and dull. The cough of pneumonia is deeper and the sputum viscid and rusty. The chest is not enlarged, the vocal fremitus is often intensified in the dull region, and the heart and liver are not displaced. The dulness on percussion is not absolute as it is in pleurisy, and the resistance to the finger in the latter is greater. The semitympanitic resonance on percussion in pleurisy with large effusion characteristically exists above the level of the fluid. In rare cases a tympanitic sound on percussion is perceived in pneumonia, but it is then most pronounced over the consolidated lung. In pneumonia loud bronchial respiration is heard over the whole of the consolidated portion of the lung, but in pleurisy with large effusion, excepting in infancy and childhood, a tubular quality of breathing is rarely heard below the level of the fluid. There may be bronchial respiration in the dull area when a slight pleuritic effusion exists, but it will not be accompanied with bronchophony but with egophony, a state of voice rendered bleating by the interposition of a layer of fluid between the costal and pulmonary pleura.

The presence of pus in the pleural cavity is to be suspected when the temperature rises and assumes a persistent remittent form, the patient at the same time often complaining of a sense of chilliness. An auscultatory sign of value is the non-transmission to the ear of the whispered voice through the fluid (Bacilli) sign ("pectoriloquie aphoniquë"). The only positive means of determining the character of the fluid is by exploratory puncture.

Hydrothorax is distinguished from pleurisy by the absence of fever in the former and by the fact that simple transudations are usually bilateral and are frequently associated with dropsy in other parts of the body. I have had the opportunity of observing three cases of unilateral serous transudation into the pleural cavity: one the result of circulatory pressure of a cancerous growth in the mediastinum and two from the pressure of enlarged bronchial glands in Hodgkin's disease.

Acute primary pleurisy in robust subjects usually ends in recovery without leaving serious after effects. But secondary pleurisies are always serious according to the gravity of the infection with which they are associated. In the treatment of the early stage, pain is much relieved by strapping the affected side of the chest or by the local application of a cold compress. When the patient dreads the cold, or if its application fails to keep the pain in check, hot flaxseed poultices, frequently changed may be substituted. An occasional

hypodermic injection of morphin gives additional comfort. The patient should be kept absolutely quiet in bed on restricted diet, until the decline of the fever. Internal medication is indicated by special symptoms. Diaphoretics are sometimes useful for modifying the pyrexia in the early stage of the disease. After the decline of the fever, the effusion having apparently reached its maximum, and when scanty secretion of the kidneys is still an existing symptom, the exhibition of diuretics is called for to stimulate absorption of the fluid. The bowels should also be kept freely evacuated, administering, if required, saline laxatives occasionally preceded by calomel followed by a purgative. The operation of thoracentesis should be performed in all cases in which the pleural cavity is largely filled with fluid, and in others with excessive dyspnea or when signs of absorption fail to appear. The internal and external use of iodin and finally of muriated tincture of iron will hasten absorption of fluid and inflammatory thickening of the pleuræ.

Pus in the pleural cavity should be promptly removed by free incision and rib resection to establish free drainage. An unexpanded lung and consequent retraction of one side of the chest are subject to improvement or cure by pulmonary gymnastics and systemitized exercise of the body in general.

RECURRENT PNEUMOTHORAX: REPORT OF A CASE, WITH REVIEW OF THE LITERATURE.

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Medical literature is replete with studies of pneumothorax, and although cases of presumed spontaneous pneumothorax are not specially common, the subject has been well considered. In attempting to ascertain the frequency of recurrent pneumothorax we found that little had been written concerning it. In Albutt's *System*,[1] Finlay says that "as a curiosity attention may be directed to recurring pneumothorax: these cases are accompanied by few symptoms, nearly always recover, and may therefore be due to rupture of emphysematous bullæ." Neither in Osler's *Modern Medicine*[2] nor in Nothnagel's *Encyclopedia of Practical Medicine*[3] is even mention made of this phase of the subject under the general head of "pneumothorax."

In 1888 Gabb[4] reported a case which he had seen in one attack

[1] Albutt and Rolleston, 1909, v, 575.
[2] Walter R. James, iii, 868.
[3] O. Rosenbach, Pneumothorax, p. 972.
[4] Recurrent Pneumothorax, British Med. Jour., 1888, ii, 178.

of pneumothorax. The patient, a female, had had three preceding attacks and had been under the care of Dr. Byrom Bramwell and his father. Her age at the time of the first attack, fourteen years previous, was forty-two. She had also had bronchitis and pleurisy of the right side in addition to the attacks of pneumothorax. In this case the pneumothorax had appeared on the same side each time. In the first attack air filled the entire right pleural cavity, but in the second the pneumothorax was localized and limited. Dr. Bramwell had been unable to find any evidence of tuberculosis, but stated that the family history was bad. One sister had a well-marked phthisis at the time of the patient's first pneumothorax. Byrom Bramwell advanced the theory that the first attack was due to the pulling upon an adhesion at the right apex during violent effort, so rupturing the lung. As the air was absorbed a friction rub appeared. Three of the attacks were on the same side. The location of one is not stated.

In 1892 Vitvitski[5] saw a young man, tailor by occupation, who complained of shortness of breath, cough, and general weakness. The family history was unimportant, except that his father died at the age of forty years of tuberculosis. A year preceding this illness the patient had noted cough and pain in the chest. His pains were temporary at first, but his health soon became so much impaired that he had to give up his occupation. At one time there appeared very suddenly dyspnea, with considerable pain in the left chest. This shortness of breath, however, passed in a few days. Two months previous to his admission to the hospital he began to have diarrhea and vomiting after taking food. Physical examination showed that he had a left-sided pneumothorax with cavity formation on the right side, well-marked signs of general pulmonary tuberculosis, and tuberculosis of the kidney. He died eight days after admission to the hospital, and the clinical findings were confirmed by the autopsy. Examination of the left chest showed not only a pneumothorax but a scar in the pleura, the size of a lentil evidently the location of the perforation of the preceding pneumothorax.

In 1898 Finny[6] recounted the history of a young man whom he had observed in two different attacks. His age at the time of his first admission to the hospital in 1897 was eighteen. The pneumothorax was on the left side. He was discharged from the hospital about five weeks later. During the absorption of air, dry pleurisy appeared. Two weeks after his discharge he reappeared at the hospital, with return of the signs and symptoms on the same side. There is no record of subsequent observation. It is of interest to note that no family history of tuberculosis was obtained.

[5] A Case of Recurring Unilateral Pneumothorax, Vrach, St. Petersburg, 1894, xv, 960.

[6] Dublin Jour. Med. Sci., 1898, cv, 273.

In 1907 Sale[7] reported a remarkable case which had come under his observation. The patient, a young woman, aged twenty-two years, had had eleven attacks of pneumothorax. In her case there was no history of familial tuberculosis. The first attack was preceded by a period of coughing and spitting of blood. There had been no fluid in the chest at any time. He did not consider that a tuberculosis infection was the causative factor.

In 1908 Hamilton[8] reported the subsequent course of 4 cases of pneumothorax whose histories had been given in a previous article. One of these cases had two attacks of pneumothorax, both on the right side. Ten years after the last attack the patient was in good health and had had no recurrence of the condition. There was nothing in this case which Hamilton considered indicative of a tubercle infection. He was under observation eleven years.

The following case came under my observation: J. H., unmarried male, aged twenty-three years. To my personal knowledge he had been in excellent health since childhood. In the family history the only significant point was the fact that his only brother had suffered at one time, some years previously, from a tuberculous elbow. This had healed after immobilization. His father and only sister were in good health. His mother died of cardiac disease. He walked to my residence on February 13, 1912, complaining of severe pain in the right side. It appeared suddenly the same day while taking his morning bath. He had been in the enjoyment of his usual good health. Temperature 98° F., pulse 80, respiration 20. There was no evident dyspnea. Physical examination at once showed that the left side of the chest was distinctly more voluminous than the right. The supraclavicular space and the intercostal spaces on this side were filled out and the intercostal depressions were not visible. Respiratory movement was slight on both sides. On the affected side, tactile fremitus was absent, while the breath sounds were distant, high-pitched, of metallic quality, with inspiration and expiration of about equal duration and intensity. The heart was pushed over to the right, the right border of dulness being 5 cm. to the right of the midsternal line and the left border being 8 cm. to the left of the same line in the fifth interspace. The point of maximum cardiac impulse was in the sixth interspace, 4 cm. to the left of the midsternal line.

Aside from the pain in the chest the patient felt perfectly well and wanted to be out. He did not seem to be ill. He was sent home and kept at rest, but would not remain in bed. February 15 his general condition remained excellent. The white blood cells were 12,000 per c.mm. Examination of the chest showed that the left side was full and immobile. The lower border of the resonance was in the ninth interspace in the axillary line and in the eleventh

[7] Lancet, 1907, ii, 1572.
[8] Spontaneous Pneumothorax, Montreal Med. Jour., 1908, xxxvii, 492.

interspace in the scapular line. I was unable to demonstrate the coin sound.

On February 18 the patient developed a complicating follicular tonsillitis, in consequence of which the temperature rose to 101.4°. The chest showed decided change. Pulmonary resonance was demonstrated at the usual points. The heart had resumed practically its normal position. The breath sounds were fairly well heard over the entire left chest except at the base posteriorly. A distinct friction rub was heard in the lower portion of the axilla and below the heart when the patient was in the reclining posture. On February 21 (eight days after onset) the physical signs had largely disappeared. The friction rub in the axilla was less and the breath sounds were not so distinct. The patient resumed his usual duties as a surveyor in about three weeks after the onset of the pneumothorax. Frequent examinations failed to show any deviation from normal.

July 13, 1913, the patient consulted me again, complaining as before of pain in the chest. This had come on suddenly. The left chest looked much fuller than the right, but it moved well on respiration, and this time the heart was not displaced. Over the entire left chest the percussion note was slightly tympanitic except at the left base posteriorly, where it was dull. Over the entire left chest the breath sounds were very distant, except over the base posteriorly, where they were absent. Tacticle fremitus was lessened throughout; over the base it was absent. No adventitious sounds were heard.

July 19 the patient reported that the pain was less. The physical findings, however, were about the same.

July 24, Drs. W. C. Hill and G. F. Thomas made stereoscopic Roentgen-ray plates. They showed a pneumothorax on the left side with what was evidently a band of adhesions running between the right pleura and the pericardium. Shadows seen in the right chest were considered by Drs. Hill and Thomas to be caused by foci of healed tuberculosis. The patient was then reëxamined very carefully. On percussion the note over the apex of the right lung proved to be slightly shorter in duration and higher in pitch than normal. An expansion of 1.5 cm. was present at the apex. The breath sounds were normal except for slightly high pitch. Vocal and tacticle fremitus were normal throughout the right lung. No rales were heard anywhere.

August 7, the twenty-fifth day after onset, the patient reported that he suffered practically no pain. Physical examination showed that the signs of pneumothorax had practically cleared up. Resonance was the same on both sides and breath sounds were transmitted as well on one side as the other, with the exception that over the right apex posteriorly, resonance was somewhat deadened. On expansion the right apex did not move as freely as the left. Since this time the patient has been examined frequently.

July 23, 1914; no deviation from normal could be detected anywhere. His weight is and has been for some months at his normal maximum. He feels perfectly well, looks well, and is engaged daily in his occupation.

August 18, 1914, Drs. Hill and Thomas again made a Roentgen-ray picture, which showed normal relations between pleura and lungs. The amount of presumed tuberculous involvement was the same as in the previous finding.

In discussing this history my own conclusion is that a dormant tubercle infection explains the etiology. In favor of this view we have Roentgen-ray plates demonstrating the existence of apparently healed foci and the presence of slight though definite physical signs at one apex, together with a transitory, dry pleurisy. The band of adhesion running between the right pleura and the pericardium, as reported by the roentgenologist, is extremely interesting in connection with the theory advanced by Byrom Bramwell in one case (Gabb).[9] One is forced to admit that the continued good health of the patient weighs heavily against this theory. It is quite possible, however, that the pneumothorax has served in this case, and perhaps in all the other reported cases but one, as a therapeutic measure, and that its occurrence has tended to retard the flaring up of a slight tuberculous focus.

In analyzing the reports, which comprise all that I have been able to discover in the literature, we see that the accompanying history gives a total of six cases. Of this number four had only two attacks (Vitvitski,[10]; Finny,[11] Hamilton[12]), but of the three one was observed but a short time and one died. One case (Gabb)[13] had four attacks and one had eleven. In some instances only a few months elapsed between the disappearance of air in the pleural sac and its reappearance, while occasionally one or two years intervened.

It is of interest to note that in one case the time elapsing between the first attack and the fourth was fourteen years, and that Sale's[14] case had all of her eleven attacks in six years.

We can find no positive evidence that more than one side was affected in any instance. It is stated by Gabb[15] that the right side was the seat of the trouble three times. The location of one seizure is not noted. Finny,[16] Vitvitski,[17] and Hamilton[18] specify that the trouble made its second appearance on the same side. Sale[19] states that three attacks were on the right side, but fails to note the location of eight. The fact must have some significance in considering the pathology, and does not bear out the theory advanced by certain writers that so-called idiopathic pneumo-

[9] Loc. cit.
[10] Loc. cit.
[11] Loc. cit.
[12] Loc. cit.
[13] Loc. cit.
[14] Loc. cit.
[15] Loc. cit.
[16] Loc. cit.
[17] Loc. cit.
[18] Loc. cit.
[19] Loc. cit.

thorax is due to the rupture of emphysematous vesicles. If this were true the condition would be expected to affect the two sides impartially.

One case only, the one which terminated fatally, presented undeniable signs of infection with tubercle. Another had a family history of tuberculosis, and had had bronchitis and pleurisy in the interval between two manifestations of pneumothorax. A third case gave a history of cough and bloody expectoration preceding her first pneumothorax. One case showed Roentgen-ray findings pointing to tubercle infection. In the remaining two cases there was no apparent valid reason for suspecting the presence of a latent tuberculosis.

Conclusions regarding the etiology of recurrent pneumothorax would be out of place with so little data at hand. It is reasonable to suppose that it is the same as in cases of "spontaneous" pneumothorax. The etiology of this condition has been quite thoroughly discussed, West[20] making the point that tuberculosis is always the causative factor. This series of cases, with four showing definite or suggestive signs of tubercle infection, is not without interest.

A CLASSIFICATION AND ANALYSIS OF CLINICAL TYPES OF SPLENOMEGALY ACCOMPANIED BY ANEMIA.[1]

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Chronic splenomegaly, usually associated with anemia, is not an uncommon condition both in adults and children. The forms without leukocytosis, more or less related to "splenic anemia," it is my intention to consider here, omitting the types of enlarged spleen in which other features render differentiation easy (such as leukemia, pseudoleukemia, polycythemia, and those secondary to obstruction or infection, as in heart disease, typhoid, kala-azar, syphilis, and so forth).

Splenic Anemia. The connection between chronic enlargement of the spleen and marked anemia without leukocytosis, as denoted in the term "splenic anemia," was first established forty-eight years ago by Gretzel,[2] in Griesinger's clinic, in Berlin. He described the

[20] Samuel West, Pneumothorax, Lancet, 1897, i, 1264.

[1] Being part of an address read before the Joint Meeting of the Pediatric Societies, New York Academy of Medicine, November 5, 1914.

[2] Ein Fall von Anemia Splenica bei Einem Kind, Berl. klin. Woch., 1866, ii, 212.

case of a child, ten months old, suffering from dysentery and severe anemia, with considerable enlargement of the spleen and lesser enlargement of the liver and lymph nodes. Examination of the blood showed that the proportion of white to red cells was not increased—that is, that it was not leukemia. Five years later H. C. Wood[3] described a "splenic variety" of pseudoleukemia, with a report of a case with a greatly enlarged spleen, severe anemia, and without leukocytosis. It must be remembered that at this time not only was pathological anatomy in its infancy, but also no exact methods existed for examining the condition of the blood. A term, therefore, like "splenic anemia," which a half century ago was a distinct advance in differentiating a new type of disease, but which now is known to include several distinct types, should now either be properly restricted or discarded entirely. By restriction I mean limitation of the term to the earlier or precirrhotic stages of Banti's disease, with which it is apparently identical. The fact that in most cases the etiology or pathogenesis of this group of diseases is not yet clearly understood is no more an argument for continuing to group them under such loose terms as "splenic anemia" or "splenomegaly with anemia" than it would have been to group typhoid with typhus fever until the discovery of the Bacillus typhosus. Though much still remains to be learned in regard to them, and though probably even their present eponymic or cumbersome names are only temporary, nevertheless it has already become more profitable to deal with them as independent affections. The inconvenience resulting from the present use of the term "splenic anemia" is quickly demonstrated to anyone making a critical survey of the literature. Statistical summaries, including valuable detailed information, are thus frequently rendered useless when, on analysis, they are found to include several independent types.

Recently evidence has been put forth to show that these conditions are perhaps related to other commoner diseases, such as pernicious anemia, various hemolytic anemias (Dibothriocephalus latus and uncinariasis), thrombosis of the portal vein or artery, and some splenic types of cirrhosis of the liver. It will be beyond my scope to more than indicate such relations. The better differentiated of these offsprings of splenic anemia are Banti's disease, Gaucher's disease (or large-celled splenomegaly), v. Jaksch's pseudoleukemia infantum, the Hayem-Widal or acquired form of hemolytic jaundice with splenomegaly, and the Chauffard-Minkowski or congenital or hereditary form of the same. I have indicated some of the differential points of these diseases in the following table:

[3] On the Relation of Leukocythemia and Pseudoleukemia, AMER. JOUR. MED. SCI., 1871, lxii, 373.

TABLE I.—DIFFERENTIAL DIAGNOSIS.

	Etiology.	Pathology of spleen.	Family history.	Time of onset.	Duration.	Icterus.	Splenomegaly.	Hemorrhages.	Anemia	Resistance of red blood cells.	Reticulated red blood cells.	Urobilinuria.	Leukocytes in blood.	Liver.	Treatment.
Gaucher's disease	Toxin ? Infection ? Tumor?	Peculiar cell hyperplasia	Occasionally positive	Childhood	Many years	Rare	+++	Occasionally	Slight	?	?	?	−	+	Splenectomy ?
Banti's disease	Toxin ? Infection ?	Hyperplasia fibrosis	Negative	Adult life	Few years	Rare	+	Occasionally	Slight to severe	Normal	Normal	+	−	First + Later −	Splenectomy.
v. Jaksch's disease	Rachitis ?	Hyperplasia fibrosis	Negative	Infancy	Several months	Rare	++	?	Slight to severe	?	?	?	+	+	Splenectomy ? Iron, arsenic, etc.
Hayem-Widal	1. Primary ? 2. Secondary to infection	Congestion and pigmentation	Negative	Any age	Many years	Present	++	Rare	Severe	Diminished	Increased	+	−	+ or normal	Splenectomy.
Chauffard-Minkowski	Heredity	Congestion and pigmentation	Positive	Congenital or childhood	Many years	Present	++	0	Slight	Diminished	Increased	+	−	+	Splenectomy.
Pernicious anemia	Enterogenous toxin ?	Fibrosis	Negative	Adult life	Few years with remissions	Very rare	Slight or diminished	Rare	Severe	Increased	Increased	+	− or +	Normal	Iron, arsenic, etc. (splenectomy questionable).

GAUCHER'S DISEASE. Gaucher's disease, or large-celled splenomegaly, was probably the first variety to be differentiated on account of its peculiar anatomical picture. Although in reality possessing little in common with the other forms of splenic anemia, I will consider it in some detail on account of the similarity of the clinical picture and from the fact that it is still included by many writers under this heading. First described by Gaucher,[4] in 1882, as a primitive epithelioma it was later shown not to possess the characters of malignancy. Bovaird[5] called it a simple hyperplasia and Brill and Mandlebaum[6] showed that it arose simultaneously from the endothelium of the spleen, lymph nodes, and bone-marrow. The characteristic large vesicular cells, with small eccentric nuclei, blocking the sinuses of the spleen and lymph nodes or crowded in the capsules of the liver lobules should make the diagnosis easy at autopsy. Careful analysis by the last-named authors, however, with rejection of falsely diagnosed cases, has reduced the number of reported cases to fourteen. Since that time five apparently true cases have been reported by Knox and Wahl[7] and Hermann.[8] Brill and Mandlebaum's excellent summary reveals the following clinical picture: The disease begins insidiously in infancy or childhood (usually before the thirteenth year) and pursues a chronic course (average of twenty years). As in some of the other varieties a history of similar trouble in the family is frequently elicited. No great disturbance in the health of the individual occurs until the disease has persisted for some time, when distinct anemia appears and, as in Banti's disease, a definite tendency to submucous or subcuticular hemorrhages. These, however, are never fatal, and death usually occurs from an intercurrent affection. The most prominent symptom is the progressive enlargement of the spleen, which may reach greater proportions than in any other disease, eventually filling most of the abdomen. The abdominal discomfort produced by the enlarged spleen may be the first indication of the disease. As in Banti's disease the blood changes are not very characteristic. The anemia of chlorotic type is never very severe (average red blood corpuscles count of advanced cases being 3,700,000). A definite leukopenia is usually found, though the differential count remains unchanged. No enlargement of the superficial lymph nodes can be found, and jaundice and ascites are rarely present. Liver enlargement, succeeding that of the spleen, may eventually reach considerable proportions.

[4] De l'Epithelioma Primitif de la Rate, Thèse de Paris, 1882.

[5] Primary Splenomegaly, Endothelial Hyperplasia of the Spleen, AMER. JOUR. MED. SCI., 1900, cxx, 377.

[6] Large-cell Splenomegaly (Gaucher's Disease), AMER. JOUR. MED. SCI., 1913, cxlvi, 863.

[7] A Case of Primary Splenomegaly of the Gaucher Type, Med. Rec., 1914, lxxxvi, 606.

[8] A Case of Gaucher's Disease, Med. Rec., 1914, lxxxvi, 606.

A brownish discoloration of the skin has been noticed with a "peculiar yellowish wedge-shaped thickening of the conjunctivæ, commonly seen on both sides of the corneæ." In spite of the rather negative character of the symptoms the disease has been recognized three times during life, with confirmation of the diagnosis by histological examination.[9]

Its etiology is still in doubt. Malignancy having been discarded, various theories of endogenous toxins, splenic enzymes, or of infection have been offered, but supported by very little evidence.

In regard to the bearing of experimental spleen work on this disease, but few facts exist to help us. Splenectomy has been tried in nine cases, with three deaths. This probably represents too high a mortality, but, on the other hand, a cure could hardly be expected, as the disease is known to exist independently in bone marrow and lymph nodes. The resistance of the red cells and number of skeined cells (as evidence of blood regeneration), as far as I can find, has not been studied, but in view of the absence of signs of increased hemolysis, one would not expect to find any noteworthy changes in such examinations. The red bone marrow, usually found at autopsy, on the other hand, would point to efforts at regeneration. As the splenic tissue is largely replaced by the peculiar Gaucher type of cell, it may be that this stimulated marrow is equivalent to that found experimentally after splenectomy.

Summing up: this disease, in spite of being frequently included among other forms of splenic anemia, has but little in common with them clinically, beyond the chronically enlarged spleen and anemia. Pathological examination should always admit its proper diagnosis to be made.

In the past few months, under the title of "an unknown disease picture," Niemann[10] has described a form much resembling Gaucher's disease, but running an acute course, with fatal termination after fifteen months. The finding of similar large endothelial-like cells at autopsy make it probable that an acute form of this disease must also be recognized.

BANTI'S DISEASE. For the more common condition of Banti's disease, or splenomegaly with hepatic cirrhosis, a brief summary will suffice to recall its general symptomatology. First described by Guido Banti[11] in 1894 the clinical picture presented at that time still holds. Usually occurring in young otherwise healthy adults, and running a chronic course, its symptomatology may be divided into three periods: in the first or pre-ascitic period, usually lasting

[9] While this paper was in press, Bernstein has reported (Jour. Am. Med. Assoc., 1915, lxiv, 1907) a fourth case diagnosed by clinical symptoms, and confirmed before operation by splenic puncture.

[10] Ein unbekanntes Krankheitsbild, Jahrb. f. Kinderheilk., 1914, lxxix, 1.

[11] La Splenomegalia con Cirrosi Epatica, Lo Sperimentale, 1894, Ses. Biol., xlviii, 407.

several years, a gradually increasing weakness and pallor are noticed with digestive disturbances and abdominal pain, which may first call attention to the enlarged, smooth, hard spleen. A tendency to hemorrhages with a moderate anemia of chlorotic type is usually present, but may be postponed until the later stages. There is nothing specially characteristic in the anemia, the increase of urobilin being the only sign of increased blood destruction. The resistance of the red cells is unchanged; signs of a regenerating bone marrow (nucleated and reticulated red cells) are slight or absent. After splenectomy, however, such changes may be noted. In such a case that I have recently had occasion to examine the red cells showed the most marked increase in resistance that I have seen clinically (complete hemolysis did not occur even at 0.25 per cent. NaCl). Though no nucleated reds were present in the circulation, reticulated forms were more numerous than before splenectomy. A slight leukopenia is characteristic. The second, or intermediate, stage lasts but a few months, is characterized by scanty, high-colored urine, containing an excess of urobilin; and by attacks of dyspepsia and diarrhea, with slight increase in the size of the liver. The third stage is ushered in by the symptoms of cirrhosis, a recurrent, painless ascites, occasionally slight jaundice, shrunken liver, and increasing anemia and emaciation. After a few years an intercurrent infection or fatal hemorrhage terminates the scene. The first two of these periods are identical with the "splenic anemia" of adults. It is hardly necessary to say that such a picture is subject to variation, and that in some cases these three periods cannot be distinguished.

In spite of the great amount of work done on Banti's disease in the past twenty years its pathogenesis is still undetermined. Except for a recent statement by Gibson[12] that he had found streptothrix in certain cases of enlarged spleen resembling Banti's disease, its etiology is still unknown. Yates, Bunting, and Kristjanson[13] have found diphtheroid organisms in several cases of Banti's disease, and consider the condition closely related to that of Hodgkin's disease. An apparently identical syndrome can be brought about by thrombosis of the portal or splenic vein (Edens,[14] Goldmann[15]), and similar clinical pictures have followed various infections, local trauma, etc. Hollins[16] has recently produced a similar condition in rabbits with injections of Bacillus coli. Banti, who first considered the enlarge-

[12] On Certain Causes of Splenomegaly and Banti's Disease, Proc. Roy. Soc., 1914, vii, Med. Sect., 7.

[13] The Etiology of Splenic Anemia or Banti's Disease, Jour. Amer. Med. Assoc., 1914, lxiii, 2225.

[14] Ueber Milzvenenthrombose, Pfortaderthrombose und Bantische Krankheit., Mitth. a. d. Grenzg. d. Med. u. Chir., 1907, xvii, 59.

[15] Zur Kasuistik der Milzvenen u. Pfortaderthrombose, Deut. med. Woch., 1913, xxxix, 1542.

[16] Primary Splenomegaly or Splenic Anemia, Practitioner, 1915, xciv, 426.

ment of the spleen to be primary, later stated that the infectious agent was brought by the artery either as a direct toxin or as a substance which, from the pathological splenic metabolism, was changed into a splenotoxin. The theory has never been confirmed by facts. The unquestioned improvement, however, that results in many cases after splenectomy, proves that the altered spleen is at least an important pathogenetic factor. This is still further emphasized by Umber's[17] interesting observation: during splenectomy for Banti's disease in a boy, aged fifteen years, a small piece of the enlarged liver was excised for histological examination and a distinct peripheral infiltration found. After the operation the liver quickly returned to normal size, a strong indication of the splenogenous origin of the hepatitis which, if undisturbed, would have progressed to the usual cirrhosis. In metabolic experiments on this patient, Umber found a nitrogen deficit that was changed to a nitrogen balance by splenectomy. This, however, has not been confirmed by later authorities.

In the pathology of the disease there is nothing specially distinctive. The enlarged spleen usually shows an increased amount of fibrous tissue in the capsule and reticulum known as "fibro-adenie" (that is, increased fibrous tissue, but retaining an adenoid appearance), and involving both pulp and follicles. The Malpighian follicles, especially in the later stages, are small and scarce; in the earlier stages they may be hyperplastic and the "fibro-adenie" be absent. Macrophages, increased amount of pigment, and other evidences of increased blood destruction are usually found. The changes in the liver are those of an ordinary periportal cirrhosis.

In summarizing, one might say that although the etiology of Banti's disease is unknown, and may well be from several sources, evidence points to the close causative relationship of the spleen. One would not expect the removal of the largely fibrotic organ of the later stages to be attended with marked somatic changes, and it is precisely in the earlier stages of the disease in which splenectomy has proved most beneficial.

Von Jaksch's Disease. The anemia infantum pseudoleukemica of von Jaksch is in all probability not an independent condition, but represents an atypical response of the infantile hemopoietic system to one of the primary diseases of the blood (leukemia, pernicious anemia, the secondary anemia of rickets, syphilis, or the formerly unrecognized types of hemolytic jaundice). A high-grade anemia, with blood picture somewhat resembling pernicious anemia, appears in infants of one or two years. The smooth, hard spleen is conspicuously large, while the liver, in contrast to the liver of leukemia in childhood, is slightly enlarged. Benjamin has lately found rickets present in

[17] Zur Pathologie der Bantischen Milz Krankheit, Münch. med. Woch., 1912, lix, 1473.

all of a series of such cases examined by him, and suggests the name "Rachitische Megalosplenie." That von Jaksch's disease is being less and less regarded as a separate disease is shown by its gradual disappearance from the text-books.

HEMOLYTIC JAUNDICE. The acquired and congenital or familial types of hemolytic jaundice with splenomegaly (Hayem-Widal and Chauffard-Minkowski) are frequently grouped by English and American authors under such titles as hemolytic jaundice (Thayer),[18] chronic family jaundice (Tileston).[19] As the two forms possess several rather important and characteristic differences, however, I have deemed it advisable to follow the continental custom and consider them as independent conditions. Search for their true etiology and pathogenesis is more apt to be stimulated under such an arrangement than if they are grouped together. Furthermore, Widal, Abrami and Brulé,[20] experimenting with toluylendiamin, have offered evidence that the two types are of different origin.

They have been so recently differentiated that they can be best considered together in their historical development. Although Murchison,[21] Wilson,[22] and others had previously described cases of chronic jaundice occurring in several members of a family (in Murchison's case splenomegaly is not mentioned), a more complete description by Hayem,[23] in 1898, was the first to establish an independent clinical condition. The clinical picture of the five cases analyzed by him was as follows: All five exhibited a chronic jaundice, with the presence of bile pigment in the blood serum, but not in the urine (*i. e.*, acholuric icterus). The other signs of obstructive jaundice, such as itching, bradycardia, and clay-colored stools, were also lacking. A distinct anemia, the red-cell count varying from 1,000,000 to 3,000,000, was present in all. Very large, hard spleens were found in each case and slight enlargement of the liver was also noted. Exacerbations were frequent, in which the jaundice deepened and bile appeared in the urine. The importance of these exacerbations was emphasized by Widal, who termed them "crises of deglobulization," and considered them highly characteristic of the acquired form. In severe cases the blood count may drop below 1,000,000, and hemoglobin appear in the urine. In all five of Hayem's cases the family history was negative, and in three the jaundice was stated to have appeared first in adult life.

[18] Hemolytic Jaundice, Illinois Med. Jour., 1911, xix, 174.

[19] Chronic Family Jaundice, AMER. JOUR. MED. SCI., 1910, cxxxix, 847.

[20] Pluralité d'Origine des Ictères Hemolytiques, Bull. et Mém. Soc. Méd. des Hôp. de Paris, 1907, xxiv, 1354.

[21] Case of Hereditary Jaundice and Gout, "Diseases of Liver," 1885, p. 481 (3d ed.).

[22] Some Cases Showing Hereditary Enlargement of the Spleen, Trans. Clin. Soc., London, 1890, xxiii, 162; ibid., 1893, xxvi, 163.

[23] Sur un Variété Particulière d'Ictère Chronique, Ictère Infectieux Chronique Splenomegalique, Presse Méd., 1898, i, 121; Nouvelle Contribution à l'Etude de l'Ictère Infectieux Chronique Splenomegalique, Bull. et Mém. Soc. Méd. des Hôp. de Paris, 1908, xxv, 122.

Two years later Minkowski[24] described a similar disease occurring in eight members of one family in three generations. This has subsequently proved to be commoner than the acquired form. In addition to the symptoms of Hayem's cases an increased amount of urobilin was noted in the urine. Autopsy revealed no cirrhosis of the liver or obstruction of the bile passages. The spleen showed a diffuse hyperplasia and hyperemia. Pigment deposits were numerous in the kidneys and centres of the liver lobules.

The next important contribution to the clinical picture of these diseases was made by Chauffard,[25] who showed in the congenital type that the resistance of the red-blood cells to hypotonic salt solution was much diminished. This simple test, suggested in 1903 by Ribierre,[26] has proved so useful in our experimental work that I take the liberty of describing it briefly:

A series of twelve or more tubes containing 1 c.c. of different strengths of hypotonic salt solution are arranged varying from 0.25 per cent. to 0.6 per cent. (or even stronger if diminished resistance is suspected). Into each one drop of whole blood is introduced and the tube gently shaken. If the drops have been of different size, occasionally slightly more blood may be added until the color is the same in all. After standing two hours at room temperature, in the stronger solutions in which no hemolysis has occurred, the unchanged corpuscles at the bottom of the tube will be overlaid with colorless salt solution. In the weakest solutions all corpuscles will have been hemolyzed, forming a transparent red solution. In the intermediate tubes can be noted at which strength hemolysis begins and at which it is complete. In normal cases, hemolysis begins at about 0.45 per cent. and is complete at 0.35 per cent. In a case of the familial type that I recently had occasion to examine, hemolysis began as high as 0.7 per cent. and was already complete at 0.475 per cent. Widal, Abrami and Brulé showed that in some cases of the acquired form, with apparently normal resistance, fragility could be demonstrated if the cells were washed free of plasma. Later work, however, has shown that any change, when present, is in the cells themselves.

Increased number of microcytes and of reticulated red cells by methods of vital staining were found by Chauffard[27] in the congenital, or familial type, and their presence later confirmed also in the acquired type. In the case above mentioned I found about 5 per cent. of the red cells reticulated as opposed to the normal of

[24] Ueber einem Hereditärischen unter dem Bild eines Chronischen Ikterus mit Urobilinurie, Splenomegalie und Nieren Siderosis verlaufende Affecktion, Verh. der Deut. Kong. f. inn. Med., 1900, xviii, 316.

[25] Pathogenie de l'Ictère Congenitale de l'adult, Semaine Méd., 1907, xxvii, 25; Les Ictères Hemolytiques, Semaine Méd., 1908, xxviii, 49; Pathogenie de l'Ictère Hemolytique Congenitale, Annales de Méd., 1914, i, 1.

[26] L'Hemolyse et la Mesure de la Resistance Globulaire, Thèse de Paris, 1903.

[27] Loc. cit.

less than 1 per cent. In some cases the figures have run as high as 20 per cent. Although Chauffard used pyroninmethyl green stain and Widal, polychrome methylene blue, we have obtained the best results with brilliant cresyl blue. A few drops of blood are dropped into a small test-tube containing a weak solution of the stain, with a little potassium oxalate to prevent rouleaux formation. After standing ten to fifteen minutes some of the sediment is pipetted off and a fresh cover-slip preparation made. The percentage of the reticulated to the non-reticulated forms is then estimated under oil immersion. If the reticulated cells are increased it is generally considered evidence of more active blood formation.

Another diagnostic method, the auto-agglutination test, is advocated by Widal, Abrami and Brulé.[28] This test consists merely of mixing one drop of the patient's washed red blood cells with ten drops of his own serum in a watch-glass. If positive, after some seconds, the mixture loses its homogeneous aspect, forms visible granules of agglomerated corpuscles on agitating, and finally, after several minutes, forms a distinct pellicle that sinks to the bottom and does not mix with the clear serum on shaking. They have found it always positive in the acquired form and always negative in the congenital or familial type. In the case I have previously mentioned this test proved negative. However, in Micheli's[29] carefully studied case of the acquired type this test was also negative. Isohemolysins have occasionally been found in both types (Micheli;[30] Hopkins[31]) but are not supposed to possess any pathological significance. Although both types of hemolytic jaundice usually run a chronic course, Gaisböck[32] has shown that an acute malignant form may occur that is fatal in a few months.

Therefore, the cardinal symptoms of these types of hemolytic jaundice with splenomegaly are found to be a chronic enlargement of the spleen, existing with an acholuric, non-obstructive jaundice, and anemia, frequently paroxysmal in character and varying in intensity. Increased blood destruction is indicated by increased urobilin in the urine, and various characteristic changes are found in the blood. The red cells show diminished resistance to hypotonic salt solution, increased number of reticulated cells with vital staining, and in the acquired form the phenomenon of auto-agglutination of the red corpuscles. The blood serum rarely contains auto- or isohemolysins.

[28] Auto-agglutination des Hematies, dans l'Ictère Hemolytique Acquis, Comp. Rendu. Soc. de Biol., 1908, lxiv, 655; Les Ictères d'Origine Hemolytique, Arch. des Mal. de Cœur, 1908, i, 193.

[29] Unmittelbare Effekte der Splenektomie bei einer Fall von Erworbenem Hemolytischen Splenomegalischen Ikterus, Wien. klin. Woch., 1911, xxiv, 1269.

[30] Loc. cit.

[31] Two Instances of Chronic Family Jaundice, Amer. Jour. Med. Sci., 1913, cxlvi, 726.

[32] Beiträge zur Klinik hemolytischer Anämien mit herabgesetzter osmotischer Erythrocyten Resistenz, Deut. Arch. f. klin. Med., 1913, cx, 413.

I have purposely postponed until now a consideration of the differentiation of the acquired and familial types and their relation to other conditions, such as those suggested by Gilbert[33] and Banti.[34] The fact that in the acquired group the disease is definitely acquired in adult life, whereas in the other there is a family history of the same trouble would not in itself be sufficient to warrant the formation of independent disease pictures. There are, however, other features which tend to differentiate their appearance more strongly. In the congenital form the subjects, as Chauffard puts it, "are more icteric than sick." Frequently they come for treatment for other conditions and consider the chronic jaundice as a family idiosyncrasy not interfering with perfect health. The acquired form, on the other hand, is usually ushered in with a definite attack of illness, the anemia becomes much more grave, sometimes as low as 1,000,000, and the patient is distinctly more anemic than jaundiced. In De Castello's[35] case, that showed great improvement after splenectomy, the red-cell count had previously fallen to 800,000.

In an analysis of 158 cases of hemolytic jaundice in which blood counts were available, I found 55 belonging to the acquired type and 103 to the congenital or familial type. Of these 103 only 23 failed to give a positive family history, whereas of the 80 familial cases 35 developed after birth. The average red-cell count of the 55 acquired cases was 2,032,000, the counts ranging from 510,000 to 4,500,000. (Counts below 1,000,000 were recorded in 10 cases, below 2,000,000 in 27 cases, and over 4,000,000 in only 4 cases.) The average count of the 103, congenital and familial, was 3,340,000, the counts ranging from 1,800,000 to 5,700,000. (N. B.—One familial case reported by v. Krannhals[36] showed 1,000,000 red cells in a single count, but as the hemoglobin was between 55 and 65 per cent. the accuracy of the count is questionable. No counts were recorded below 1,000,000, 8 below 2,000,000, and 25 above 4,000,000. The average of the familial cases was 3,281,000; of the congenital, 3,543,000.) These figures show that there is a much more marked anemia in the cases of the acquired type than in the familial.

Widal and his pupils claim that the auto-agglutination test is only positive in the acquired form, and considers it important evidence that the two diseases have fundamentally different origins. I have already called attention to the differential importance of

[33] Cholémie Familiale, Bull. Mém. Soc. Méd. des Hôp. de Paris, 1907, xxiv, 1203. (N. B.—This contains references to all of Gilbert's work on this subject to date.)

[34] La Splenomegalia Emolitica, Patologica, 1911, iii, 471; La Splenomegalia Emolitica Anemopoietica, Sperimentale, 1913, lxvii, 323.

[35] Discussion of Kahn's case, Verhand. d. deut. Kong. f. inn. Med. (Wiesbaden), 1913, xxx, 331.

[36] Ueber Congenitale Ikterus mit Kronischem Milztumor, Deut. Arch. f. klin. Med., 1904, lxxxi, 596.

Widal's "crises of deglobulization," although it must be admitted that marked fluctuations are present also in the familial type.

Cases have been reported where a condition apparently identical with the acquired form under discussion has followed attacks of malaria, syphilis, and other infections, and further study will probably reveal that all cases of this type are due to more or less obscure intoxication. The signs of excessive blood destruction usually disappear from these cases when the underlying cause is successfully treated. The familial form, on the other hand, appears more as an inherited dystrophy of the hemopoietic system, rendering the red-blood cells more easily destructible. On this basis Chauffard at first strongly advised against splenectomy in this type, but subsequent cases have shown such improvement after this treatment that it would seem as if the removal of this site of blood destruction was advisable, whether or not it is the primary seat of the trouble. After Kahn's[37] and Roth's[38] successful splenectomies of the familial type the resistance of the red cells failed to return to normal.

The congenital type, with negative family history, grouped with the familial type by most authors, has less grounds for differentiation from the acquired form. The mere fact that the disease has already made its appearance at birth is of itself not of fundamental importance if there is no history of similar trouble in the family. I feel, therefore, that if the familial form (which, as a matter of fact, is usually, though not always, congenital) were opposed to the acquired form, the time of onset, as indicated by the term congenital, might well be disregarded. The possibility of an early acquisition of the disease is shown in the case reported by Beneck and Sabrazés.[39] With a negative family history, a suckling acquired the disease apparently from her wet-nurse, who, together with her two children, had a chronic hemolytic jaundice. Certain authors consider the two types identical. Hynek,[40] for instance, bases his opinion on two cases observed by him, the mother acquiring the disease after childbirth, whereas with her child it appeared congenitally. Plehn[41] reports a case appearing congenitally in father and daughter, but not until the twenty-sixth year in the case of a son. Benjamin and Sluka[42] observed three

[37] Ueber Hemolytischer Icterus und Seine Behendlung durch Splenectomie, Verh. d. deut. Kong. f. inn. Med., 1913, xxx, 326.

[38] Ueber die Hemolytische Anämie, Deut. Arch. klin. Med., 1912, cvi, 138; Der Angeborene Hemolytische Ikterus, Corresp. Schweiz. Aerzt., 1913, xliii, 689.

[39] Ictère Hemolytique Chronique, Avec Splenomegalie, Gaz. Heb. Sci. Méd. de Bordeaux, 1909, xxx, 469.

[40] Chronischer Ikterus mit Milztumor ohne Bilirubinurie, Casopis Lekaru, ceskych., 1906, p. 1029. (Ref. Schmidt's Jahrb., 1907, ccxciv, 160.)

[41] Familial Milz und Leber Vergrösserungen mit Anämie, und Gutartiger Verlaufung, Deut. med. Woch., 1909, xxxv, 1749.

[42] Chronische Acholurische Icterus mit und ohne Milztumor, Berl. klin. Woch., 1907, xliv, 1065.

cases in one family, two appearing congenitally and one in adult life. Many of these could undoubtedly be harmonized if the time of onset was disregarded.

In favor of the identity of the two types it must be admitted that a series of cases could be selected in which many grades between the two types could be represented. It is obvious also that the familial type must at one time or another have originally been acquired. In such an event the difference in severity between the acquired and familial still holds. Thus both in Roth's[43] and Bychorski's[44] cases the disease in the parent who acquired it was severe, while in the children who inherited it, it was of the usual mild type. Such facts, however, would not indicate a fundamental difference in the nature of the two diseases.

In the small number of cases already accumulated, various atypicalities have been reported. Thus, Lommel's[45] and Claus and Kalberlah's[46] cases of the familial type, and Mosse's[47] and Tixier's[48] cases of the acquired type failed to show any change in resistance of the red cells (either washed or of the whole blood), though other evidences of increased blood destruction were present. In a few cases also a similar acholuric jaundice with splenomegaly has existed together with polycythemia instead of anemia. A slightly different form has also been described by Chauffard and Vincent,[49] Van den Bergh[50] and Roth,[51] in which homolysins are present in the blood, which, so to speak, occupies a midway position between hemolytic jaundice and paroxysmal hemoglobinuria "a frigore." Gibert[52] and his pupils have published numerous reports since 1900 on similar conditions under the name of "cholemie familiale." They have at least served to call attention to the fact that variations may be found in the amount of enlargement of the spleen and liver. It is questionable, however, if it is necessary, as they have frequently done, to consider each atypical form as a separate condition to be dignified with a separate name. As many of their cases were described before the various hematological methods above described had come into vogue, and are frequently reported in resumé, it is difficult

[43] Loc. cit.

[44] Zur Kasuistik der Heredofamiliaren Splenomegalien, Wien. klin. Woch., 1911, xxiv, 1519.

[45] Ueber die Sogenannte Bantische Krankheit und den Hemolytischen Ikterus, Deut. Arch. f. klin. Med., 1912, cix, 174.

[46] Ueber Chronischen Icterus, Berl. klin. Woch., 1906, xliii, 1471.

[47] Zur Lehre der Krankheiten mit Gesteigertem Hämolyse, Berl. klin. Woch., 1913, l, 684.

[48] Ictere d'origine Hemolytique, Resistance des Hematies Desplasmatisées Sensiblement Normale, Comp. Rendu de la Soc. de Biol., 1908, lxiv, 43.

[49] Hemoglobinurie Hemolysinique avec Ictère Polycholique Aigu, Semaine Méd., 1909, xxix, 601.

[50] Ictère Hemolytique avec Crises Hemoglobinuriques, Fragilité Globulaire, Rev. de Méd., 1911, xxxi, 63.

[51] Zur Frage des "Ictère Hemolysinique" (Chauffard), Deut. Arch. klin. Méd., 1913, cx, 77.

[52] Loc. cit.

to tell for sure whether or not they should be considered as belonging to the types under discussion. Their theory of hepatic origin, due to an infectious angiocholitis, was later abandoned by them in favor of Chauffard's idea that the primary change was in the blood.

All the symptoms of increased blood destruction may be present and yet icterus be absent. Thus, Chauffard describes a family in which the mother is a typical hemolytic icteric, while the eighteen-year-old son presents all the signs except the jaundice.

When the anemia is grave the blood may present a picture indistinguishable from pernicious anemia (v. Stejskal).[53] Chauffard considers that there is an icteric form of pernicious anemia which, when accompanied by diminished resistance and reticulated red cells, represents the least compensated form of hemolytic icterus. Widal and Weissenbach[54] have also reported a case of this type. In the usual Biermer type of pernicious anemia, icterus is absent and the resistance of the red cells increased.

Banti[55] has recently proposed the name hemolytic splenomegaly for a type of case which on analysis is indistinguishable from the acquired form of hemolytic jaundice. The two cases described by him (one an aplastic subvariety) both exhibit a chronic anemia, with long-standing splenomegaly, subicterus, diminished resistance of the red cells, increased number of reticulated cells, and urobilinuria. The beneficial effects of splenectomy, abolishing the anemia and changing the resistance to normal—in one case even changing an aplastic into a reacting bone marrow—lead him to ascribe a primary role in this disease to the spleen. It must be remembered, of course, that removal of the normal spleen indirectly causes an increase in resistance of the red cells. Banti claims never to have seen Widal's crises of deglobulization in these patients, and emphasizes the presence of a relative lymphocytosis; but this would hardly indicate a different disease. As to the choice of name, Banti's is open to the same objection as the other, namely, that splenomegaly may be absent in some cases (Le Gendre,[56] Pick,[57] Gilbert,[58] Benjamin and Sluka's third case, and Marchiafava and Nazzari[59]) just as jaundice is in others. A name indicating increased blood destruction, such as hemolytic hypersplenism, without including individual features, would be less open to

[53] Uber Hemolytischen Icterus und uber den Auftreten Hemolytischen Vorgänge bei diesem und bei Perniciöse Anämie, Wien. klin. Woch., 1909, xxii, 661.

[54] Anémie Pernicieuse Cryptogenetique avec Hemolysinhémie et Fragilité Globulaire Alternante, Bull. et Mém. Soc. Méd. Hôp. de Paris, 1913, xxix, 250.

[55] La Splenomegalia Emolitica, Sperimentale, 1912, lxvi, 91; La Splenomegalia Emolitica Anemopoietica, Sperimentale, 1913, lxvii, 323.

[56] Deux observations d'Ictère Hemolytique l'un Congenitale l'un Acquis, Bull. et Mém. Soc. Méd. Hôp. de Paris, 1909, xxvii, 112.

[57] Ueber hereditärischem Ikterus, Wien. klin. Woch., 1903, xvi, 493.

[58] Loc cit.

[59] Sugli Itteri Emolitici, Bull. d. Reale Accad. di Roma, 1909, xxxv, 152.

objection; but in the meantime the name sanctioned by usage is preferable.

PATHOGENESIS. As I have already indicated in the discussion of the differentiation of the two types, an hepatic or luetic etiology has been largely discarded for the idiopathic primary types. There remain the two views, that the primary lesion is in the blood, a dystrophy of the red cells; or either primarily or indirectly in the spleen, an exaggerated hemolytic activity. Widal and his school, the extreme supporters of the former view, consider that the congenitally weak red-blood cells are destroyed in the circulation and their remains taken up by the spleen (causing a spodogenous tumor) and by the liver, kidney, and bone marrow (hence the excessive pigment found in these organs at autopsy). This view was supported by Vaquez,[60] von Stejskal, Benjamin and Sluka, Aschenheim[61] and Weber and Dorner.[62] The chief objection to it is that it completely ignores the great improvement following splenectomy. A primary increased hemolytic activity of the spleen as the source of the malady was first proposed by Minkowski and supported by von Krannhals and Chauffard. Its latest adherent, Banti, as I have previously stated, considers that the pathological spleen not only is spodogenous, but actively destroys increased numbers of cells and prepares others for destruction. Though based on incorrect and inadequate experimental evidence; this attractive combination of the splenogenous and hemocatatonistic theories at present seems most plausible. Although it is not possible to demonstrate hemolysis by the normal spleen, we cannot exclude the possibility that that organ may in such diseased conditions, as Banti claims, take on increased hemolytic activity. Extracts from the spleens of Antonelli's[63] and Kahn's[64] cases, however, failed to show any hemolytic activity.

Whatever the source of the increased blood destruction may be, there results an increased amount of hemoglobin to be got rid of. The majority of authorities believe that it is changed by the liver into bile in excessive amounts, viscid and highly pigmented, which clog the bile capillaries, are resorbed into the blood, and thus cause a "pleichromic icterus." Recent investigations by Whipple,[65] however, show that bilirubin can be formed by the action of endothelium of bloodvessels entirely isolated from the hepatic circulation.

[60] Ictère chronique acholurique avec splenomegalie, Bull. et. Mém. Soc. Méd. Hôp. Par., 1907, xxiv, 1184; Sur l'Anatomie Pathologique de L'Ictère Hemolytique, Arch. des Mal. de Cœur., 1908, i, 609.

[61] Ueber Familiären Hämolytischen Ikterus, Münch. med. Woch., 1910, lvii, 1282.

[62] Four Cases of Congenital Acholuric So-called Hemolytic Jaundice in One Family, Lancet, 1910, i, 227. Acquired Chronic Acholuric Jaundice, AMER. JOUR. MED. SCI., 1909, cxxxviii, 24.

[63] Intorno all'Effetti della Splenectomia su Ittero Emolitica Acquisita con Anemia a Tipo Perniciosa, Policlinico (Par. Med.), 1913, xx, 3.

[64] Loc cit.

[65] Icterus, Jour. Exp. Med., 1913, xvii, 612.

If this be true a hematogenous icterus in the narrower sense can be accepted. That the jaundice is not due to gross obstruction is proved by the facts that such obstruction has never been found, that the stools are of normal color, and that the urine does not contain bilirubin.

It is interesting to note that in Banti's aplastic or anemopoietic case, splenectomy started the regenerating powers of the bone marrow as shown by the appearance of normoblasts in the circulating blood. This would indicate that with the spleen there was removed a toxin that had inhibited blood formation and would argue that the weakened red cells of hemolytic jaundice are due, not to hemocatatonistic action of the spleen, but to an indirect injury to the bone marrow.

PATHOLOGY. Of the comparatively few cases that have come to autopsy or splenectomy a study of the morbid anatomy has not been very productive. I have collected eight autopsies and seven splenectomies, with the results shown in table on opposite page.

THERAPEUTICS. Views as to the treatment of these conditions have changed fundamentally in the past few years. Following Vaquez and Giroux's[66] case, in which death ensued two days after splenectomy, came Chauffard's dictum that hemolytic jaundice constituted a "Noli me tangere" for the surgeon. Various surgical attempts on the bile passages (Chauffard and Troisier;[67] Marchiafava and Nazzari; Widal, Abrami and Brulé); *x*-rays (Benjamin and Sluka); bone marrow feeding (Chauffard, Widal); cholagogues (Chauffard, Cavazza)[68] all proved unavailing. Only with a long-continued course of iron diet did Widal find some improvement. On account of the antihemolytic properties of arsenic (Gunn and Feltham)[69], cholesterin (Chauffard and Grigaut,[70] Parisot and Heully[71]), and calcium chloride (Iscovesco[72]), these drugs have been tried, in some cases with improvement, apparently due to increasing the resistance of the red cells. No curative measure had been produced, however, when splenectomy was again tried in 1911, with very different results. In that year Micheli removed the spleen from a case of the acquired type, with the most striking improvement; the blood count which had been between 980,000 and 2,600,000 quickly rose to almost normal, the acholuric jaundice and urobiliburia disappeared, the fragility of the red cells was lessened, and the patient within a few months was apparently

[66] Ictère chronique acholurique avec Splenomegalie, Bull. et Mém. Soc. Méd. Hôp. de Paris, 1907, xxiv, 1184.

[67] Des Rapports de Certaines Anemies Splenomegaliques avec L'Ictère Hemolytique Congenitale, Bull. et Mém. Soc. Méd. des Hôp. de Paris, 1909, xxvii, 293.

[68] Gli Itteri Emolitici-Milano, 1911.

[69] The Antihemolytic Power of Arsenic, British Med. Jour., 1911, i, 134.

[70] Le Taux de la cholesterinemie au cours des cardiopathies, Comp. Rend. Soc. Biol., 1911, lxx, 108.

[71] Le Traitement des Ictères Hemolutiques, Semaine Méd., 1913, xxxiii, 85.

[72] Les Lipoides du Sang. La Cholesterine, Comp. Rend. Soc. Biol., 1908, lxiv, 404. See also ibid., 1907, lxiii, 744.

TABLE II.—PATHOLOGY OF HEMOLYTIC JAUNDICE.

Author.	Type.	Based on	Weight of spleen.	Capsule and trabeculæ.	Pulp.	Sinus.	Malpighian follicles.	Pigment in spleen.	Phagocytes in spleen.	Pigment in liver.	Bone marrow.	Miscellaneous.
Minkowski .	Familial.	Autopsy.	Gms. 675	Normal.	Congestion.	Congestion.	...	Increase.	Increase.	Increase.	Red.	Much pigment in kidneys.
Vaques and Giroux . .	Familial.	Autopsy.	850	Normal.	Marked congestion.	Congestion.	Normal.	Increase.	Increase.	Normal.	Red.	
Gandy and Brulé[73]	Familial.	Autopsy.	750	Normal.	Marked congestion.	Congestion.	Normal.	Slight increase.	Increase.	Normal.	Red.	
Marchiafava .	Familial.	Autopsy.	270	Thick.	...	...	Necrotic.	Increase.	...	Increase.	...	Spleen slightly fibrotic.
Oettinger[74] .	Acquired.	Autopsy.	575	Normal.	Marked congestion.	Congestion.	Small.	Increase.	Increase.	Increase.	Red.	Much pigment in kidneys.
Micheli . .	Acquired.	Autopsy.	850	Thick.	Congestion.	Congestion.	No germ centres.	Increase.	Slight increase.	Normal.	Red.	Endothelial cells of spleen increased. Liver fibrotic.
Kahm 1 . .	Familial.	Operation.	970	Normal.	Congestion.	Congestion.	Normal.	Increase.	...	...	...	Few pulp cells in spleen.
Kahm 2 . .	Familial.	Operation.	1170	Thick.	Congestion.	Congestion.	Few.	Slight increase.				
Umber. . .	Acquired.	Operation.	1300	Normal.	Congestion.	Congestion.	Pigmented and congested.	Increase.	Increase.			
Antonelli . .	Acquired.	Operation.	1000	Normal.	Congestion.	Congestion.	Normal.	Increase.	Increase.			
Fiori . . .	Acquired.	Operation.	1000	Normal.	Marked congestion.	Congestion.	Normal.	Increase.				
Banti 1 . .	Acquired.	Operation.	1580	Normal.	Marked congestion.	Congestion.	Normal.	Increase.	Increase.			
Banti 2 . .	Acquired.	Operation.	970	Normal.	Marked congestion.	Congestion.	Normal.	Increase.	Increase.	...	...	Endothelial cells of spleen necrotic.
Gaisböck . .	Acquired.	Autopsy.	?	Normal.	Not congested.	Not congested.	?	Increase.	Increase.	Increase.	Red.	Myeloblasts in liver and spleen.

[73] Gandy, C., and Brulé, M. Ictère Hemolytique Congenitale Autopsie, Bull. et Mém. Soc. Méd. Hôp. de Paris, 1909, xxviii, 369.
[74] Oettinger, W. Sur un Cas d'Ictère d'Origine Hemolytique non Congenitale, Bull. et Mém. Soc. Méd. Hôp. de Paris, 1908, xxvi, 391.

cured. Similar beneficial results were obtained by Banti in his two cases of hemolytic splenomegaly, which I have taken to be identical with the acquired form of hemolytic jaundice. In the past two years splenectomy has been performed successfully in both acquired and familial types in cases reported by Antonelli, De Castello, Kahn, Lankhout,[75] Fiori[76] and Eppinger.[77] In no cases were there any bad results, and all showed a great improvement in symptoms, with specific evidence of lessened blood destruction. It is, of course, too early to know whether the improvement is but temporary or whether permanent cure has been effected.[78]

With such gratifying results and the analogous hyperthyroidism in mind, it is not surprising that the procedure should be applied to related conditions such as hypertrophic cirrhosis and pernicious anemia. Eppinger[79] considers that the amount of hemolysis in a given case can be determined by the iodin count of the blood fat (normal 80 to 90) and the amount of urobilin in the feces (normal 0.12 to 0.15 gm. per day). He found both these increased not only in hemolytic jaundice, but also in pernicious anemia, hypertrophic cirrhosis, and catarrhal jaundice. As he and King had found experimentally that removal of the spleen caused a great drop in the iodin content, (*i. e.*, lessened hemolysis), he proposed splenectomy in this type of case also. His latest theory of the pathogenesis of pernicious anemia is more fanciful. Having found thickened walls in the arterioles of the spleen, he assumes that the blood seeks the path of less resistance through Weidenreich's open capillaries into the pulp, where they are destroyed. Splenectomy therefore becomes equivalent to tying off a ruptured bloodvessel. This theory has not yet received widespread acceptance.

Klemperer's[80] summary of ten cases shows that the operative risk in pernicious anemia is considerable, and if successfully passed, an improvement which is not fundamental is the most to be hoped for. It is noteworthy that he bases the procedure on the incorrect hypothesis that splenectomy normally causes an increase in the number of red cells. Huber,[81] De Castello[82] and Mosse have also found im-

[75] Hemolytische Splenomegalia, Nederl. Tijd. d. Geneesk., 1913, lvii, 1153.

[76] Un caso di Splenomegalica Emolitica Trattata colla Splenectomia, Sperimentale, 1913, lxvii, 189.

[77] Zur. Pathologie der Milzfunction, Berl. klin. Woch., 1913, l, 1509 and 2409.

[78] Since the above was written, the patient to whom I have previously referred has also successfully undergone splenectomy, with great improvement of clinical symptoms and return of blood picture almost to normal. His case with metabolic studies before and after splenectomy will shortly be reported by Pearce, Pepper, and Goldschmidt. The results of splenectomy in hemolytic jaundice have very recently been collected by Elliott and Kanavel (Surg., Gyn. and Obstet., 1915, xxi, 21). Of 48 cases splenectomized, 2 have died, and in the 46 "cures," practically all symptoms of the disease have disappeared.

[79] Loc. cit.

[80] In welcher Krankheit Kommt die operative Entfernung der Milz in Frage? Ther. d. Gegenwart, 1914, lv, 1.

[81] Ueber die Blut Veränderungen bir Icterus Hemolyticus, Berl. klin. Woch., 1913, l, 681 and 2179.

[82] Ueber den Einfluss der Milzextirpation auf der Perniciöse Anamie, Deut. med. Woch., 1914, xl, 639.

provement after splenectomy in an icteric type of pernicious anemia. It is interesting that in Huber's case the blood cells from the splenic vein showed no decrease in resistance. As all three patients had icterus, urobilinuria, fragility of corpuscles, and splenomegaly it is probable that these cases really belong to the class of hemolytic jaundice.

One might say in summarizing that splenectomy should be considered in all those diseases where there is evidence of increased blood destruction and that in early Banti's disease and hemolytic jaundice at least the results of splenectomy have been execllent. All such procedures, however, should be entered upon most conservatively as long as so much of the physiology of the spleen remains unknown. Though its removal is known to be compatible with life, it may yet prove to have such important detoxicating relations to infection or to digestion, that splenectomy should only be practised after most careful study and to relieve the most serious conditions.[83]

CULTURAL AND VACCINE RESULTS IN A CASE OF HODGKIN'S DISEASE.

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In the number of the *Archives of Internal Medicine*, for August, 1913, Bunting and Yates report six cases of Hodgkin's disease, from the lymphatic glands of which they have isolated a diphtheroid organism considered by them as identical with the one described by Fraenkel and Much.[1] In 1900 the last-named authors were able to extract Gram-positive, non-acid-fast, diphtheroid bacilli from the sediment of the lymph glands which had been previously treated with antiformin, to which preparation the organism was resistant.

Negri and Miermet[2] were the first to report successful cultivation of this organism, isolation of which was brought about on Bordet's medium (blood-glycerin-potato-agar).

Billings and Rosenow[3] have isolated the same organism from eighteen cases of Hodgkin's disease, the glands of which were

[83] Since the above was written, numerous reports of splenectomy for pernicious anemia have appeared. Though the patient's general condition was improved temporarily in many cases, in no case has definite cure resulted, or the blood picture of pernicious anemia been fundamentally changed.

[1] Ztschr. f. Hyg., 1910, xvii, 189.

[2] Centralblatt f. Bak., 1913, lxviii, 292.

[3] Jour. Amer. Med. Assoc., December, 1913.

diagnosed microscopically. The majority of the cases show the glands to be of the endothelioid type described by Reed and Longcope. They report favorable vaccine results in some of the cases, practically all of which were simultaneously treated with the Roentgen-ray. This agent, as is well known, often causes decrease in the size of the cervical glands, but as a sequel to this treatment the thoracic and retroperitoneal nodes seem to develop faster.

Since every case of this disease that reacts favorably or unfavorably to an autogenous vaccine is of value, I feel justified in reporting this single case, even though my vaccine results are distinctly unfavorable:

The patient under consideration was a male, aged fifty-seven years. He had worked as a carpenter all his life. He was first seen May 8, 1915, and gave the following history: About one year ago he noticed a stiffness in the back of his neck which could never be made to disappear completely, and which was aggravated by slight chilling. Three months later he noticed a gland under the right tonsil somewhat enlarged, and accidentally discovered two small kernels in the occipital region. In February, 1914, other glands appeared on the right side of the neck, with a beginning involvement in a similar location on the opposite side. They had all been of rapid growth, were painless, and were freely movable under the skin. The tonsils were not greatly enlarged, and no history of repeated tonsillitis or sore throat was obtainable. The Wassermann reaction, urinalysis, and von Pirquet test were negative. The blood findings were as follows: reds, 4,900,000; whites, 10,200; hemoglobin, 89 per cent. A differential count of 500 cells shows: polymorphonuclears and transitionals, 62 per cent.; lymphocytes, 20 per cent.; large mononuclears, 14 per cent.; eosinophiles, 4 per cent.; no myelocytes or basophiles. No pathological changes in the red cells.

May 8, 1914, a lymphatic gland, with capsule intact, was removed from the right submaxillary region under local anesthesia. This will be known as R I. It measured 2 x 3½ cm., and had been growing for about three months, attaining most of its size in the last month.

On the left side the most recently involved gland was removed. It was located at the level of the cricoid cartilage under the sternomastoid. An incision was made in this muscle, and under moderate pressure from the forceps this gland, which was decapsulated, accommodatingly popped up through the incision. Its size was 1 x 2 cm. It was transferred directly to a tube of whole blood glucose agar. It will be known as L I. There was also removed from the same location a circular node recently involved, and about 6 mm. in diameter. It will be known as L II.

A pathological examination of the glands showed the following changes: For the most part the histological architecture of the

gland was destroyed. There was marked lymphoid hyperplasia in addition to a striking hyperplasia of the endothelial cells lining the lymph sinuses. A few multinucleated bizarre-shaped endotheliod giant cells were present, but no eosinophiles were observed. A diffuse sclerosis was just beginning. In some parts of the early nodes the arrangement of the gland had not been disturbed, and the proliferation of the endothelial cells lining the sinuses gave the appearance of densely packed cords of cells. In other areas only the lymphoid hyperplasia was noticeable.

Gland R I was washed in sterile normal salt solution and transferred to a sterile Petri dish. It was longitudinally incised and divided into three parts. The following disposition was made of the sections: A suitable portion was placed in formalin for pathological examination, the result of which has just been described. A second portion was placed in a sterile mortar and ground in sterile air. An emulsion was made in sterile normal salt solution and was planted on fifteen tubes of different kinds of media. The results of these cultural findings are not detailed in this article because they were the same in substance as were derived from the third portion of the gland, the results of which are detailed in the protocol. This portion was cut into small pieces and planted on several tubes of the following kinds of media: (1) 2 per cent. glucose agar, plus 10 per cent. beef serum; (2) 2 per cent. glucose bouillon plus 10 per cent. beef serum; (3) 2 per cent. glucose agar plus 5 per cent. whole human blood; (4) 2 per cent. glucose bouillon plus 10 per cent. ascitic fluid; (5) 2 per cent. glucose agar plus 5 per cent. whole human blood, about three weeks old. These media were incubated forty-eight hours before their use in these experiments. For the sake of convenience and brevity these different varieties will be referred to as Media 1, Media 2, etc., in the protocols.

An examination of the protocols of the cultural results discloses several things of interest: The marked pleomorphism of the organism has been mentioned by Bunting and Yates, and it is indeed one of its striking as well as its confusing features. Some of the diphtheroids are very large, these usually being club forms or ones heavily barred. Others are short and thick, corresponding to the solid type of the diphtheria bacillus. Under certain conditions the coccoid forms of varying size and staining power are developed. Branching forms were not uncommon. Some have a long, terminal filament, usually wavy in character. This may branch, or it may give rise to a more or less complex network which when stained by Gram's method is easily decolorized. Many of the coccoids have shorter spicules or projections of this character, while the wavy, pale filaments may also be seen free in the smears, and which show the above-mentioned characteristics. All these forms usually disappear in the transplants. The filaments are interesting in rela-

tion to the supposed spirochetes seen by Proescher and White[4] in Hodgkin's glands, and thought by them to be the etiological factor in the disease. Their observations have not been generally confirmed. These filaments may also throw light on the origin of the spirochetes of Vincent's angina. They have never been cultivated, and are supposed by Tunnicliffe[5] to be outgrowths of the fusiform bacillus of this condition. They can usually be seen as thin, wavy filaments attached to one end of the bacillus in a well-stained preparation.

There was considerable variation in the gross features of the cultures. On blood-agar the growth began, as a rule, in the water of condensation. It grew slowly on the slant, appearing for the most part as a moist dewdrop formation, thus resembling the Streptococcus pyogenes. Later it turned a light gray color and grew more luxuriantly. It had a decided preference for a moist surface. It would lie dormant for some time on the surface of a dry medium, but would grow readily when a little distilled water or sterile salt solution was added to the medium. Not infrequently the individual transplanted colonies would become opaque with unequal intensity, giving the colony a stippled appearance. On beef serum and plain glucose agar the growth was slow and sparse, but became more luxuriant with frequent transplants. The cultures gradually became chromogenic, producing first a yellow and later an orange or pink pigment. One culture transplanted May 26, 1914, in gelatin was viable December 1, having developed an orange pigment. The bacillus was decidedly aërobic, spreading arborescently over the surface of the gelatin in sunflower fashion, while the beaded growth along the stab had not perceptibly progressed. The viability was best preserved on gelatin.

Bouillon was diffusely clouded during the first few hours of growth, but soon cleared up, giving rise to a moderate quantity of fine granular sediment, collecting along the sides and on the bottom of the tube. When beef serum was added to the glucose bouillon the tendency for the organisms to clump was quite noticeable.

Neither glucose nor lactose was fermented, nor was a trace of acid produced even when using such a delicate indicator as Andrade's reagent[6] (decolorized acid-fuchsin).

The organism was resistant to antiformin and was non-acid fast. It stained faintly in Loeffler's, but easily with gentian violet and carbolfuchsin. The best differentiation was brought about by the method of Gram, to which it reacted strongly under favorable conditions. But any change of environment had a remarkable effect on its power to retain this stain.

[4] Münch. med. Wchnschr., 1907, liv, 1868; Jour. Amer. Med. Assoc., 1907, xlix, 1115.

[5] Jour. of Infect. Dis., 1906, iii.

[6] Annual Report United States Marine Hospital Service, 1895, p. 385.

In general it can be said that the growth on old blood agar and on dry media caused a large number of the organisms to be decolorized. In the condensation water of cultures a week old such changes could easily be seen. In some cultures all grades of reaction to this stain might be seen; in others, the entire culture was finally decolorized. Prolonged growth on the simple media was also favorable for the retention of this stain. However, when the coccoid bodies were developed by any of these processes they were much more constant in their positive reaction to the Gram stain than were the bacilli. The reasons for these deductions can be seen by consulting the protocol.

May 15, 1914. L I.
May 14, 1914. Transplant 2.
May 21, 1914. Transplant 11.
May 15, 1914. L I, both slant and water of condensation.
May 15, 1914. Transplant 19, L I.
May 16, 1914. Transplant 26, L I.
May 13, 1914. Transplant 8, L II.
May 22, 1914. Transplant 31, L I, condensation water.

Another point of interest toward which attention was directed, lay in determining whether the cocci or coccoid forms were derived from the bacilli or represented a separate bacterium. By first shaking up the organisms with sand, and then plating them out by the dilution streak method, isolated colonies containing no coccoids were found. When transplanted under unfavorable conditions, an abundance of these forms appeared. (See plate cultures I, II, and III, under subcultures of gland L I.) In addition it will be seen that gland L I and L II contained none of these when the growth first started. By following the examinations of the condensation water of L I from day to day a progressive shortening of the organism was seen, until finally many of these anomalous forms appeared. One tube of gland L II which had contained no coccoids, ran along for several days without change, either macroscopically or microscopically. Then from May 15 to May 16 the growth suddenly changed from a transparent dewdrop character, to a more luxuriant opaque formation. Microscopically, practically nothing but coccoids were found. (See L II, May 16.) Other reference to protocols bearing on this point are transplants No. 3, May 12 and May 14; transplant No. 16 of May 14; transplants Nos. 14 and 15, of May 18.

It seems probable that the coccoids represent involution forms of the bacillus, as they flourish under an unfavorable environment. If, for example, the organism grows on a medium which delays its appearance, or on a stale or dry medium, coccoids appear quickly. The age of the cultures also has a decided bearing, especially if it be on one which degenerates rather rapidly, *e. g.*, blood agar. (Under L I protocol, see description under date of May 13

and May 15 (Plate I). Transplant II of May 21, 1914; transplant 19 of May 15, 1914; transplant 25; transplant 35 tube (3) of L I, May 18, 1914; under L II see transplant 8, and under R I see tube number 5, May 15, 1914; transplant 9 of May 12, 1914.

Attempts to have the coccoids develop in chains failed. (Transplants 40 and 41.) No true spore formation or motility was observed. Gelatin was not liquefied, but was the best medium among those I used to preserve the viability. Large involution spherical forms were present in old cultures of this medium, which were usually chromogenic.

No attempt was made to enter into all the details of morphology, and the cultural and biochemical characteristics which go to determine unequivocally the location of the organism in its proper place. Only those were entered into which would suffice reasonably for its identification as described by those who first isolated it. However, the apparently rare filamentous forms and its chromogenic capacity were novel to me.

PATHOGENICITY. May 18, 1914, a guinea-pig and a rabbit were each injected with a salt suspension of 1 c.c. of the bacillus from the right gland into each thigh subcutaneously. A rabbit and a guinea-pig were also treated with 1 c.c. of the suspension from the left gland. This time the injection was made subcutaneously into the right thigh, and also intraperitoneally, 1 c.c. being given in each place.

None of the animals showed symptoms, but the rabbit which received the injections in two locations soon lost the extreme vivacity which had characterized her heretofore. Progressive diminution in weight and strength occurred until October 20, 1914, at 5 P.M., when the animal died in an extremely emaciated condition. (Original weight, 1940 grams; antemortem weight, 860 grams.) No rise in temperature was observed at any time.

Autopsy, October 20, at 6 P.M. Smears were made from all organs, but were negative. Parts of the lung, liver, heart, kidneys, spleen, and ovaries were placed in formalin and subjected later to a pathological examination, which was negative. Lymphatic involvement was also negative. Parts of the organs were planted on blood agar. Results were negative except with an ovary, which after five days yielded on the slant two small gray colonies, which proved to be diphtheroids of the same character morphologically as the ones injected. The condensation water surrounding the tissue was rich in the same organism.

On transplants to blood agar the organism grew in light gray colonies after forty-eight hours. It was a strongly Gram-positive, non-acid-fast diphtheroid. It produced no acid on glucose and did not liquefy gelatin. It was decidedly pleomorphic, following the same general lines as its supposed antecedent, except that no coccoid forms have been observed up to this time.

Cultures of it have been injected daily into rabbits for a month, but so far the animals have shown no significant signs. Animal experiments with both organisms are being continued.

VACCINE TREATMENT AND SUBSEQUENT HISTORY. Vaccines were prepared from the bacilli of both glands and from the coccoid forms of the left gland cultures. The organism was grown forty-eight hours on glucose-agar, washed down in normal salt solution, filtered through glass-wool-cotton filter to remove clumps, heated to 56° for one hour, after which 0.1 formalin was added. Controlled for four days on blood agar.

May 25, at 11 A.M., five millions of the killed bacilli of gland L I were given subcutaneously into the left arm. No temperature; no local, focal, or constitutional reaction.

May 28, ten million bacilli given in the same manner. Glands of right side given a mild Roentgen-ray treatment. No reaction of any sort.

May 30. Some improvement. He turned his head more easily; all palpable glands receded slightly and the patient felt generally improved.

May 31. At 8 A.M., fifteen millions of the dead organisms from L I were given. No reaction of any kind. No improvement in his condition. In fact, the glands in the cervical region were gradually enlarging and the axillary glands on the right side, and the inguinal glands on both sides were involved. A Roentgen-ray treatment given, but no improvement resulted.

June 8. A vaccine of 25,000,000 given subcutaneously. He returned home until July 13. During this time he received three doses of vaccine, the sizes of which were 50,000,000, 75,000,000, and 85,000,000. He was not under my control at this time, but was treated by his home doctor. He reported no improvement from any of the vaccines. The dose of 85,000,000 produced a rise in temperature of 3°, which receded in forty-eight hours. The glands continued to enlarge.

July 13. I administered a dose of 150,000,000. He had only a slight temperature rise, but his condition did not change.

He did not return for further treatment, but went to Chicago some time later, where he was treated by Dr. E. C. Rosenow. From him I learned that an axillary gland had been removed and a vaccine prepared. I next heard from his home town that he died about September 1.

In this case I am unable to see any good results whatever that can possibly be traced to his autogenous vaccine, although the dosage did not go above 150,000,000. Excepting a few transitory improvements, which might be traced to the Roentgen-ray, his downward course was a rapid and uninterrupted one from May 8 until July 13, and his demise six weeks later would seem to conform to the previous rapidity with which the disease pro-

gressed. I might add that the removal of the glands by surgical operation caused a rapid enlargement of the neighboring glands. I can only hope that my case was atypical and that the general run of the cases will yield to treatment.

PROTOCOL OF CULTURAL RESULTS.

Media No. 1—Two per cent. glucose agar plus 10 per cent. beef serum. May 9, 1914: No growth. May 10, 1914. No growth. May 11, 1914: No growth.

Media No. 2—Two per cent. glucose bouillon plus 10 per cent. beef serum. May 9, 1914: No growth. May 10, 1914: The bouillon is diffusely clouded. Microscopically bacilli of varying size and shape are found. Many solid and barred types, while a few have bipolar granules. A few coccoid forms are present. Stain well with Gram but faintly with Loeffler's. May 11, 1914: A heavy white precipitate is deposited at the bottom of the tube, while the supernatant fluid is clear. No change microscopically.

Media No. 3—Two per cent. glucose agar plus 5 per cent. whole human blood. May 9, 1914: Negative. May 10, 1914: Negative. May 11, 1914: Negative.

Media No. 4—Two per cent. glucose bouillon plus 10 per cent. ascitic fluid. May 9, 1914: Negative. May 10, 1914: Negative. May 11, 1914: Negative.

Media No. 5—Two per cent. glucose agar plus 5 per cent. whole human blood (three weeks old). May 9, 1914: Negative. May 10, 1914: Negative. May 11, 1914: Negative.

Left Gland L I.

Media No. 1—Two per cent. glucose agar plus 10 per cent. beef serum. May 9, 1914: Negative. May 10, 1914: Negative. May 11, 1914: Negative.

Media No. 3—Two per cent. glucose agar plus 5 whole human blood. May 9, 1914: Negative. May 10, 1914: Negative. May 11, 1914: Negative.

Media No. 5—Two per cent. glucose agar plus 5 per cent. whole human blood (three weeks old). May 9, 1914: Negative. May 10, 1914: The cloudy fluid surrounding the piece of gland shows the same findings as occur in the bouillon from the right gland, except no coccoid forms are present. Gram-positive. May 11, 1914: Increase of turbidity in the condensation water. This was permitted to run over the slant of agar. See transplants 2, 10, 11, 19, 22, 23, 25, 26, 31, 32, 33, 35, 40, 41, 42 under protocol of subcultures, L I.

Left Gland L II.

Media No. 3—Two per cent. glucose agar plus 5 per cent. whole human blood. May 9, 1914: Negative. May 10, 1914: Negative. May 11, 1914: Negative.

Gland R I.

Media No. 1—May 12, 1914: No growth. May 13, 1914: Growth appeared for first time. Many coccoid forms. Variation in reaction to Gram stain. May 14, 1914: No change.

Media No. 2—May 12, 1914: Increase of growth. No change microscopically. See transplants 1, 3, 4, 6, 7, 9, 16, 17, and 29 under Protocol of subcultures R I. May 13, 1914: No change. May 14, 1914: No change.

Media No. 3—May 12, 1914: Negative. May 13, 1914: Negative. May 14, 1914: First growth appears. Dewdrop formation. Diphtheroid and coccoid forms. Gram positive.

Media No. 4—May 12, 1914: Negative. May 13, 1914: Negative. May 14, 1914: Negative.

Media No. 5—May 12, 1914: First growth shows fine barred and solid bacilli. Gram positive. May 13, 1914: Growth first occurred as Gram positive bacilli and coccoids. May 14, 1914: Many barred forms.

Gland L I.

Media No. 1—May 12, 1914: Negative. May 13, 1914: Negative. May 14, 1914: Negative.

Media No. 3—May 12, 1914: Tube 41 shows fine, slender, long bacilli and coccoid forms. All are Gram positive. May 13, 1914: The slant shows many coccoids. Marked pleomorphism. The condensation water shows bacilli, narrower and shorter, but maintaining the granulation. Sparcity of coccoids. May 14, 1914: No change.

Media No. 5—May 12, 1914: The slant shows a thin, grayish, slimy growth. Microscopically, diphtheroid bacteria of great diversity of size and shape. Clubs, dumb-bells, and grotesque forms. Practically all have one or more deep blue granules located at the dilated end of the bacillus. Metachromism. Loeffler's stain negative, organisms are strongly Gram positive. May 13, 1914: Tube 2, L I. All coccoid bodies. Occur singly as diplococci, or in groups. Great diversity in staining power. This is first growth on Tube 2, L I. May 14, 1914: No growth as yet on slant. Turned condensation water over slant.

Left Gland L II.

Media No. 3—May 12, 1914: Negative. May 13, 1914: All bacilli as in Tube 1, L I. Dewdrop colonies on slant. See transplants 8, 13, 14, 15, 28, 30, 34, and 38. May 14, 1914: No change.

Gland R I.

Media No. 1—May 15, 1914: No change. May 16, 1914: All are Gram-positive coccoids.

Media No. 2—May 15, 1914: No change. May 16, 1914: No change. May 21, 1914: Most of the bacilli are Gram-negative. Some Gram-positive coccoids found.

Media No. 3—May 15, 1914: Many barred forms. Positive to Gram. May 16, 1914: No change.

Media No. 4—May 15, 1914: Negative. May 16, 1914: No growth occurred.

Media No. 5—May 15, 1914: No change. May 16, 1914: No change.

Gland L I.

Media No. 1—May 15, 1914: Negative. May 16, 1914: No growth occurred.

Media No. 3—May 15, 1914: Condensation water shows many Gram-positive coccoids, and many Gram-negative diphtheroid bacilli. May 16, 1914: Condensation water of L I contained small Gram-positive, barred bacilli.

Media No. 5—May 15, 1914: Fine dewdrop growth, just starting to turn gray. Strongly Gram-positive cocci. May 16, 1914: No change.

Gland L II.

Media No. 3—May 15, 1914: Forms are shorter and more of the solid type, but still bacilli. May 16, 1914: All Gram-positive cocci. The slant is no longer of dewdrop appearance, but is light gray.

PROTOCOL OF SUBCULTURES OF GLAND REMOVED FROM THE RIGHT CERVICAL REGION (R I).

First generation of subcultures.

May 12, 1914—Transplants 1 and 3 planted May 11. From Media No. 2 to fresh whole blood agar (Media No. 3). Both tubes show some heavy gray colonies and some that look like dewdrops. The former are Gram-positive, slender, long bacilli with marked granulations. Only a few club forms. Barred type predominates if the media is a little old or dry. The dewdrop colonies show the same bacteria.

May 17, 1914—Transplants: 6 and 7 from Media No. 2 to Media No. 1. Shows a pure culture of very large bacilli with most intense barring. No coccoid forms present. Protoplasm is light blue, but the bars are intense blue. Transplant 29 is from the incubated

gland in the Petri dish on which colonies appeared first May 12. Planted on beef serum bouillon. A precipitate formed in the bottom of the tube. Supernatant fluid clear. No clumping. Shows Gram-positive coccoid forms.

May 15, 1914—Tube 5. First appearance of growth May 12. Single colony growing from a piece of gland tissue. Colony gray and has not spread laterally as much as in depth. Microscopically, short, fat Gram-positive bacilli of the solid type, as well as thinner curved Gram-negative filaments, which may or may not be bacteria.

Second generation of subcultures.

May 13, 1914—Transplant 4 from dewdrop colonies of transplant 1 to Media No. 2. Shows slender solid type bacilli. Gram-positive.

May 16, 1914—Transplant 9 from dewdrop colonies of transplant 1 to Media No. 5. Many coccoid forms mixed with slender bacilli. Variation in reaction to Gram stain. Some bacilli are greatly decolorized.

May 14, 1914—Transplant 16 from transplant 3 to Media No. 5. Shows Gram-positive barred and coccoid forms. Transplant 17 from transplant 6 to Media No. 1. Shows same forms as transplant 6. Transplant 18 from transplant 1 to Media No. 3. Dewdrop colonies. Microscopically, strongly Gram-positive, barred bacillus.

Part of right gland in Petri dish incubated at 37°, May 8. Small gray colonies appeared May 12. Mostly they are Gram-negative cocci, although a few are Gram-positive. Some colonies are very fine, slender bacilli, with coccoid forms which are Gram-negative.

Subsequent examination of previous subcultures.

May 13, 1914—Transplant 3. Still shows slender, long bacilli. Gray growth gradually becoming opaque.

May 14, 1914—Transplant 3 shows true coccoid forms, but little else. The individuals are quite large. There are many short, plump bacilli and some barred types. Compare description of same culture of May 12.

May 14, 1914—Transplant 6. No change. All Gram-positive.

May 16, 1914—Transplant 6. Very few are Gram-positive. Mostly Gram-negative, barred forms.

May 13, 1914—Transplant 1. Growth changed from dewdrop to gray, and colonies are opaquely stippled.

May 21, 1914—Tube 5, R I, transplanted to beef serum. Very slow development. Fusiform and barred types. Only moderately positive to Gram.

May 21, 1914—Transplant 17. Large, barred bacilli. Some positive and some negative to Gram.

First generation on different media.

May 12, 1914—Transplant 2 from condensation water of L I on Media No. 3 to Media No. 3. An apparently pure culture of a bacillus, uniform in size and shape, with many Gram-positive, barred forms. Transplant 10 from the condensation water of L I to beef serum. (Media No. 1.) Many barred forms and some coccoids.

May 21, 1914—Transplant 11 from L I, May 13, to old blood agar. All are cocci of varying sizes. Some Gram-positive and some Gram-negative.

May 15, 1914—Transplant 19 planted May 14, 1914, from slant of L I to Media No. 5. Shows a fine dewdrop growth. Microscopically, shows coccoids, moderately Gram-positive.

May 16, 1914—Transplant 25 from agar slant L II on Media No. 3 to Media No. 1. Mainly small Gram-positive cocci, and a few bipolar bacilli.

May 17, 1914—Plate I. May 11, 1914, a dilution streak on Petri dish of Media No. 5 from condensation water of L I. No growth until plate was moistened with salt solution. Then the individual colonies appeared along the streak. An examination of individual colonies shows Gram-positive and Gram-negative diphtheroids in the same colony.

May 18, 1914—Plate III from condensation water of L I to Media No. 3, planted May 16. Same results as on Plate 1.

May 18, 1914—Transplant 35 from condensation water of L I, planted May 12, 1914 on Media No. 5. First growth May 17, 1914. Nothing but Gram-positive coccoids.

May 18, 1914—Transplant 31. Entire gland L I transplanted to Media No. 3 on May 16, 1914. Shows diphtheroids of remarkable diversity of form. They are strongly Gram-positive. Many drumstick forms are present, the stems of which are projected into long tails which stain Gram-negative. Sometimes these whips or tails branch simply, but at other times the arborization is almost dendritic. These Gram-negative filaments are also free in the smear. They may explain the apparent Gram-negative filaments or bacteria found in the other cultures. The oval coccoids often have tails at both ends. Some are Gram-positive and others Gram-negative. They resemble early Leishmann-Donovan bodies. Transplant 35. From condensation water of L I, planted May 12 on Media No. 5. Nothing but Gram-positive coccoids.

Second generation on different media.

May 16, 1914—Transplant 26, from transplant 23 to Media No. 3. Diphtheroids and coccoids which show all grades of reaction to Gram stain.

May 18, 1914—Transplants 32 and 33 from transplant 26 on Media No. 3. About same forms as described under transplant 31, excepting there are fewer coccoids and Gram-negative filaments.

May 18, 1914—Transplant Plate II. Transferred a colony of diphtheroids from Plate I to a plate of Media No. 1. Microscopically, they are all Gram-positive cocci of varying sizes. There are some bipolar bacilli, the bodies of which stain poorly with Gram.

May 18, 1914—Transplant No. 2, transplanted to Media No. 3 from original colonies of Plate I which were cocci. Microscopically nothing but Gram-positive cocci. Transplant No. 10 is from Plate III into human serum bouillon. In eighteen hours, growth shows cocci, but merely a suggestion of chain arrangement. Nothing definite. Transplant 41 from Plate III into beef serum bouillon. A very decided clumping of the cocci occurs. No suggestion of chain arrangement.

Subsequent examinations of subcultures L I.

May 13, 1914—Transplant 2. Slender, barred bacilli in the condensation water. No change.

May 14, 1914—Transplant 2. Great variation in the reaction to Gram-stain. Many bacteria are nearly decolorized.

May 22, 1914—Transplant 31. The slant shows many branching forms of diphtheroids. Gram-positive. The shapes are more regular in the condensation water, and do not hold the Gram-stain well.

May 18, 1914—L II, tube 3, planted May 8. First growth May 15. Almost all Gram-positive cocci. Very few diphtheroids.

Subsequent examinations of subcultures L II.

May 21, 1914—L II on Media No. 2. No change. All Gram-positive coccoids.

PROTOCOL OF SUBCULTURE OF THE SECOND GLAND REMOVED FROM THE LEFT CERVICAL REGION (L II).

First generation of different media.

May 13, 1914—Transplant 8 from L II Media No. 3 to Media No. 1. Short plump forms with small amount of barring and granulation. They are not Gram-negative, but are greatly decolorized.

May 17, 1914—Transplant 28 is from slant of gland L II into Media No. 2. Precipitate in the bottom of the tube, while the supernatant fluid is clear. Shaking yields a finely granular cloud. Marked clumping tendency. Transplant 30 is from L II slant into human serum bouillon. Same findings as transplant 28.

May 18, 1914—Transplant 34. L II planted on Media No. 1, May 15. Shows Gram-positive cocci. Transplant 38, from tube 2, gland L II which showed nothing but cocci on first examination. No change in this transplant.

May 18, 1914—Transplant 13, from transplant 28 to Media No. 1. All Gram-positive cocci. Transplant 14 and 15 are from transplant 28 to Media No. 5. Small Gram-positive coccoids. Some do not hold the stain well.

THE DIAGNOSIS BETWEEN PRIMARY AND SECONDARY ACUTE CARDIAC PICTURES.[1]

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It is with a full appreciation of the intimacy of the confidence imposed upon the consultant, and of the restrictions limiting the ownership of clinical data acquired under the relations of professional privilege and friendship, that I am venturing to sketch in barest outline four cases seen recently in conference with medical friends.

The first was of a man who complained of intense dyspnea on the slightest exertion in bed, of substernal oppression, of palpitation, and of sharp precordial pain. The pulse was feeble, slightly irregular, and in rate 120. The temperature was subnormal. The cardiac symptoms had impressed his physician to the extent of leading him to minimize the fact that the patient was breathing little, if at all, with his left side, which posteriorly showed unmistakable evidence of a bronchopneumonia, from which in due course he died.

The second patient was a young woman whose pulse rate, when I first saw her, was 130 and above on the slightest exertion. Even at rest it remained constantly about 110. She had been an excessive tea and coffee drinker, and had been in the habit of frequently using headache powders. She was of a highstrung, neurotic temperament, and the victim of long indoor hours, overworry, and work. When sent to me for examination she could hardly walk from the door to a chair. Palpitation and dyspnea were distressing, and were even worse when at rest in bed than when exercising. Moderate numbness and pain at times extended down the right arm. There was no cough, no sputum, no hemoptysis. She had

[1] Read before the Section on Medicine, College of Physicians of Philadelphia, November 23, 1914.

been healthy until five weeks before. Her physician concluded that her case was one of neurasthenia. This patient's heart was found widely dilated to the right, left, and upward; both jugulars were pulsating in systole, and over the entire precordia could be heard a rough, short, systolic murmur. There was no edema. The lungs showed here and there a few subcrepitant rales due to congestion.

The third patient was a young man who presented a series of clinical symptoms very similar to the preceding, except that he was large and robust of frame, whereas patient No. 2 was thin and frail. His dyspnea, palpitation, and general physical exhaustion had increased progressively during three months, until he himself was alarmed. He had previously been strong and well. His physician, a woman, sent him to me for examination primarily in order that sexual excesses might be determined or excluded as the basal factor in the case. The clinical picture was suggestive of myocardial incompetency. The physical examination did not dispel the likelihood of this supposition. But the boy's own frank admission of excessive sex intercourse, as well as the favorable outcome of the case, left no other conclusion possible than that the myocardium was and is normal and sound when permitted to perform its functions under the influence of sane nervous stimuli in a body nourished by internal secretions which were being squandered in riotous waste.

In the fourth and last case I was asked to examine the heart with a view to the possibility of a septic myocarditis. The patient was suffering at the time from a suppurating knee-joint and a large inguinal pus collection. His pulse was 110 to 120, his temperature had just touched 105° F., he was coughing, and spitting mucus and bright red blood. On examination it was evident that his heart was widely dilated, with active venous pulsation in the neck, and marked arrhythmia. The cardiac action was angry, but there was no murmur present. Very striking, however, at the first glance were the immobility of the entire left chest as compared with the laboring right side, and the shower of subcrepitant rales heard in the left axilla. There was undoubtedly present a septic congestion or (its later stage) a central bronchopneumonia, and the cardiac embarrassment was evidently to be attributed equally to it and to the causal toxemia.

The study of the foregoing and similar cases has led me for my own benefit, as well as for the advantage of others who may be placed in similar conditions, to attempt to formulate a working scheme for the discrimination between primary and secondary acute cardiac clinical syndromes.

I shall not consider at this time the relation between the heart and the kidney, or between heart insufficiencies and sclerosis of the vascular system. These fields are too extensive and present the conditions of chronic rather than acute disease. Moreover,

their discussion would finally lead us to no definite agreement. I shall dwell briefly on such acute cardiac pictures as appear in neurotic states, in gastro-intestinal toxemias, in the pneumonias, in tuberculosis, in hyperthyroidism, in drug intoxications, and other systemic embarrassments that tend to obscure the real causal factor and to over- or underemphasize the heart.

At the close of a clinic a few days ago the question was asked, "How does it happen so often that the first signs of a pulnonary tuberculosis are heart or stomach symptoms?" This question graphically defines the aim and the limitations of this study. If we were to use slightly different words we might ask, "How often does the heart act as the spokesman for other organs; how can we make certain when it is speaking only for itself?"

There will, no doubt, be as many methods of procedure as there are individual examiners. It may even be that the most thorough and successful of all will formulate no definite scheme. If so he deserves no credit for his talent other than as the possessor of an inheritance by divine right. He is fortunate, but he has not earned his success. However, there are not many of him.

It is well to recognize the fact at the start that the discrimination is not always easy, and now and again is exceedingly trying and difficult. There are *two general conditions* in which we may find ourselves put to the test, and *two cardinal principles* upon which it appears to me rational to base our procedure. The first of the general conditions is exemplified in a patient experiencing cardiac symptoms in the presence of (though not necessarily due to) organic muscular or valvular disease of the heart. The second may be noted in one suffering from a cardiac syndrome in the entire absence of a recognized antecedent lesion, and perhaps in the presence of a heart, normal heretofore, and still normal under ordinary circumstances.

The first and by all odds the best *method* I could suggest would be a deliberate and complete ignoring of the heart in the preliminary physical examination and a studied effort to explain doubtful symptoms on other grounds than those of cardiac disease. Failing in this, and forced at length to consider the heart as the *origo et fons mali*, I would propose as the second step in the diagnosis a still further reluctance to attribute more of importance to the cardiac disease than is its due. Translated into other terms this means that we should continually remember the intimacy of the interrelation between the heart and every other of the thoracic and abdominal viscera, also the brain, and the influence of this interrelation upon the symptoms arising from these organs.

The functional integrity of every organ depends first, if not last, upon the origination of a tiny stimulus in the cardiac sinus node, upon its transmission through the several conducting pathways, and upon the heart's systolic output in suitable quantity of a nourishing blood supply. This being true, it will be easy for slight

and secondary cardiac embarrassments to announce themselves in the language of either hungry or overfed heart-dependent organs. Standing on the threshold of a thoroughgoing reconstruction of the physiology of the heart and, consequently, of the physical diagnosis of cardiac disease, our task at once takes on a perplexing and tentative nature, and our doctrines must be correspondingly circumspect.

Confusion will most often come from the respiratory side. Fastened securely to the lungs above and behind by the pulmonary vessels and the pericardial reflections, and still more firmly to the diaphragm below by its pericardial union with the wall of the inferior vena cava, the heart experiences every movement of the lungs, one or both, and, in pulmonary affections, suffers not only from too much, but from an unsuitable form of exercise. The lungs expand from the apex downward, and in their excursion carry the heart downward from its normal position. As soon as the great veins are put under traction their supply of blood to the auricles is interfered with and the equilibrium and mechanism of the cardiac cycle at once has to pay toll. This interference with the veno-auricular flow is a far more vital menace than any mere mechanical obstruction in the pulmonary tissue. There can exist no room for doubt that an excessive number of the 30,000 and more air vesicles may be put out of commission by overdistention, or by crowding with exudate, or by rupture, or by collapse due to pressure from fluid or other cause without. These are, however, not the conditions that lead to serious acute mechanical disturbances. Very seldom do they, of themselves, cause fatality. The bacteremias and toxemias that cause these states are the vital factors threatening the heart, not the consolidations and the congestions and the edemas and the transudates and exudates of fluid, as a rule. Because of this fact both the myocardium and the gastric mucosa offer their early complaint in tuberculosis and pneumonia; and, for the same reason, not infrequently, the cardiac or the gastro-intestinal picture dominates the course of the pulmonary disease. A focus of bronchopneumonia no larger than the tip of the little finger may prove a vigorous enough centre for the spread of an infection that may express itself loudest, for the reasons given, in terms of cardiac distress. The nerve and muscle cells and fibers of the myocardium are being attacked by the toxin, and the rapid and irregular respiratory movements are coincidently depriving the heart of its supply of blood. Its complaint can be heard and felt throughout the entire economy.

Our first step, therefore, is directed toward the exclusion of primary pulmonary disease.

Next in order of the important causes of secondary cardiac disabilities will be the mischief-making due to gastro-intestinal toxins. These may arise from the decomposition of an oversupply of food

or make their appearance in the form of food end-products. Eustis[2] has suggested certain of the amino-acids, especially histamin, as influential in this direction. I have no doubt he is correct in his belief. But long before Eustis or any other medical writer recorded his observations the human individual, lay and medical, was experiencing, with full knowledge of the cause, the hypertension, tachycardia, palpitation, arrhythmia, and precordial pain as the result of an overindulgence in any and every kind of food, and, in the case of certain individuals, of the most sparing indulgence in certain non-protein articles of diet rated as uniformly beneficial. I have had many an uncomfortable personal experience of this kind in the form of a toxemia, many of the expressions of which were purely cardiac and circulatory, resulting from the ingestion of an apple or an orange. An identical picture could and can be produced at any time by shell-fish or by an excess of any kind of food.

Appendicitis, acute or chronic, gastric disorders, duodenal ulcer, simple or tuberculous enteritis, the amebic infections, all spell toxemia and consequent myocardial involvement. Frequently there is added a mechanical factor in the form of tympanites to still further embarrass the involved heart. Not infrequently also there appear acute renal or pulmonary contributions, which, in their turn, burden the heart as it runs the gauntlet of this vicious circle. I have more than once had referred to me a patient with a supposed cardiac disease, whose circulatory symptoms disappeared as soon as the gastro-intestinal tract and the dietary had been subjected to the appropriate hygienic regime.

It is tempting to include the thyroid and pituitary disorders as well as the adrenal affections, and to indicate the prominence and frequency of the secondary reflections in the heart. The grave anemias, the onset of the acute infectious diseases, sepsis in any and all of its forms, may furnish pictures of an essentially cardiac hue.

The point to be emphasized here is that a heart free from antecedent disease may protest so vigorously concerning its vicarious distress as to divert attention from the true etiology and from the seat of primary involvement. It may also invite treatment that will not only prove unavailing, but detrimental, because directed at an innocent, even though a noisy and complaining target.

The second method of discrimination requires equal nicety of judgment, and precision, and thoroughness in the physical examination—namely, the weighing of the influence of a known organic cardiac disease against the secondary symptoms due to incompetency of other organs. All insufficiencies of the lungs, liver, kidneys, or gastro-intestinal tract directly dependent upon cardiac disease

[2] New Orleans Med. and Surg. Jour., 1914, p. 730.

are properly a part of the primary cardiac picture, and should be included therein. But we must sharply differentiate between the symptoms attributable to an old valvular lesion with its accompanying myocardial degeneration and those, for example, of an intercurrent infectious pneumonia; we must distinguish between the syndromes of a rheumatic endocarditis and myocarditis and the cardiac symptoms of an intercurrent gonorrhea; and, finally. we must distribute the responsibility for symptoms in the not infrequent coincidence of a persistent influenzal pneumonitis or apical tuberculosis and "rheumatic" or syphilitic organic cardiac disease. The foregoing constitute practical illustrations of the difficulty, as well as the intense interest, involved in the study of the heart in its many relations, primary and secondary.

It will be of advantage to remember that tachycardia, arrhythmia, cough, blood-spitting, and even the physical signs of acute dilatation may result from pulmonary or gastro-intestinal disease in the complete absence of primary cardiac disease. Demonstrable extension of the right, left, and upper cardiac boundaries, an extended precordial impulse, a muffling of the cardiac sounds, edema of the extremities and of the genitalia, and of the serous cavities, extreme degrees of cyanosis, precordial aching and oppression (as contrasted with sharp pain), and a markedly low systolic blood-pressure, all point to primary cardiac incompetency, both in the presence and absence of contributory symptoms originating in other organs. A high degree of arteriosclerosis in child or adult speaks, *a priori*, for an incompetent heart muscle of long standing. In the child it usually also represents a systemic hereditary syphilis. Such a paper as this might be extended indefinitely. Its value or uselessness will depend upon its success in imbuing the hearer or reader with the need of humble, painstaking care rather than haste in the final determination of the causal factor. Brilliancy, after all, should be only lightning thoroughness.

Careful history-taking is an absolute essential which merits more serious comment than is permitted by the time in hand. The study of the blood-pressure, especially with respect to excessive pulse-pressure or cardiac overload, will often enable one to avoid the error of misinterpreting an organic myocardial disease. An insistence upon the opportunity of eating at table with the patient, and keeping him or her under direct observation during several meals, will occasionally furnish the final clue, uniting and correlating the obscure train of evidently toxemic cardiac complaints.

A blood culture even in an incipient tuberculosis[3] will often afford valuable evidence of the activating factor in a disturbing cardiac syndrome.

I have said enough to attract attention to the importance not

[3] Lopatin, Russky Vratch, June 6, 1914. Nine out of sixteen guinea-pigs inoculated gave a positive tuberculosis test.

only of the ever-increasing number of instances of cardiac and cardiovascular disease, but equally to the vital necessity of separating the physical signs and symptoms that are not primarily due to cardiac disease from those that are.

We must, by every rational endeavor, avoid laying upon the heart an etiological overload in the form of secondary symptoms.

THE CAUSES OF BACKWARD DISPLACEMENT OF THE UTERUS.

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The varied symptom-complex of real or fancied injuries sustained by a railroad, trolley, or traffic accident often presents some reference to the condition of the pelvic organs, and in an examination of the pelvis in an attempt to locate the seat of the trouble a retrodisplaced uterus may be found. That such a condition may occur through an accident seems firmly fixed in the public mind, and even among the profession the idea that sudden or acute retrodisplacement of the uterus can occur through falls, straining or similar injuries apparently finds credence. So by the patient, and not infrequently by the medical attendant, the newly discovered retrodisplacement is held as the cause of the backaches, headaches, and other manifestations of the nervous breakdown or neurasthenia which often follows such an accident. With the idea of such an etiological factor for the condition, legal action to recover damages is instituted against some common carrier, railroad, or trolley line on which at a previous time the patient may have been thrown from her seat or suffered a fall from derailment or other mishap.

The question arises as to whether such a condition as acute retrodisplacement of the uterus may be produced by a sudden fall, strain, or injury. A reference to the standard text-books on diseases of women shows that while such a cause is not considered by some authors, it is mentioned by others simply to deny their belief in it, and where it is classed as a possible factor, it must be regarded as occurring only in extremely rare instances. As a rule, simple retrodisplacement of the uterus *per se* seldom if ever causes symptoms for which medical relief is sought, the accompanying pathology in most cases being responsible for the subjective symptoms. It is possible that a partially retroverted uterus or a uterus already in retroversion might by some sudden increase in pressure of the abdominal contents, as by straining or violent injury, be forced down in the pelvic cavity. In such an instance the sudden

ligamentary strain might cause immediate pelvic pain. But in many cases the pain referred to the pelvis is of muscular origin, and has nothing whatever to do with a displaced uterus. The patient previously ignorant of this condition may have noticed no symptoms resulting therefrom, but her attention will remain focussed upon it long after the real effects of the injury have passed away. It would seem that under conditions of normal tonicity the supporting ligaments of the uterus, accustomed to the actively physical life of the average woman, would hardly permit overstretching enough to allow a complete retrodisplacement of the uterus to occur.

There are many factors which influence the production of displacements of the uterus. The one most frequently noted is childbirth, with the accompanying trauma to the pelvic floor and pelvic diaphragm, the early rising after labor, with a subinvoluted uterus illy supported by the imperfectly restored ligaments, or on the other hand, the long dorsal decubitus favoring by gravity the backward displacement of the heavy uterus. Premature interruption of pregnancy, abortions, and miscarriages, so lightly considered by many as to the after-care, predispose in the same manner as labor at term. So in any claim as to the production of a retrodisplacement of the uterus through injury, the nature of any previous pregnancies, their mode of termination, and the attention received in the puerperium would be information of the highest importance.

So, too, any previous disease of the pelvis, infections, or tumors of the adnexa, and pelvic peritoneum with their resulting adhesions, changes in tone or structure of the supporting ligaments, the possibility of a metritis through contiguity, and a consequent weakening of the uterine structure through relaxation or atrophy, and tumors of the body of the uterus, may all cause retrodisplacements passing unnoticed for many months, and whose occurrence in the history of a claimant must be noted.

Congenital displacements often cause no symptoms until perhaps at puberty, when with the onset of menstruation various abnormal phenomena may occur. Or this function may be established normally and, after marriage, sterility often occasioned by the congenital retrodisplacement with its accompanying defects, acute anteflexion, shortening of the vaginal walls, and elongated and stenosed infantile cervix may lead to the first recognition of its presence. But if just previously to or about the time medical attention was required the patient suffered an accident resulting in a severe jar to the body or a fall, it will receive considerable attention as to the part it may have played in being responsible for the symptoms noted.

In order to ascertain to what extent a history of trauma in one form or other occurs in the average case of displaced uterus, I have, through the courtesy of Dr. B. C. Hirst, examined the histories of 529 cases of this condition occurring in his private practice. A

number of these cases, referred for pelvic examination as an aid in explanation of some obscure medical condition, represent accidentally discovered cases of symptomless retroposition. Childbirth at term, associated or not, with miscarriage, explains clearly the etiology of a group of 304 cases. In a similar way we can ascribe a previous miscarriage or miscarriages as causing the condition in a second group of 33 cases. The diagnosis of pregnancy or the abnormal symptoms resulting from pregnancy in a retrodisplaced uterus explains the discovery of the displacement in a group of 16 women. There remain two groups, one of 81 sterile married women, and a final one of 88 single women. The total number, 169, of these two groups seems rather high when one considers that childbirth is given as the most common etiological factor by most authorities. In but few of these cases of single or sterile married women was there a simple mobile retroplaced uterus. Some additional pelvic pathology, inflammatory disease of the adnexa, recent or old, and with adhesions, evidences of previous pelvic peritonitis, cystitis, appendicitis, and so on was usually present.

In 13 cases, slightly over 2 per cent. of the whole number of cases, a history of accident or trauma was found. In the first instance the patient had suffered a fractured hip by being thrown from a carriage several years previous to the pelvic examination, which was requested on account of dysmenorrhea and leucorrhea. As this condition followed a period of normal menstruation of four years after the carriage accident, and as she had been informed while undergoing treatment in another city that no displacement existed, it must seem impossible that the accident played any part in the production of this displacement. In the second case a single woman, aged twenty-eight years, menstruation began at twelve years of age. At this time she suffered a fall and was said to have injured her coccyx; for this injury she stayed in bed six weeks. She complained chiefly of pains in the lower abdomen resembling menstrual cramps, which she said followed a second fall received a month previous to the examination. A complete retroversion was found. It would be difficult to say which, if either, of the falls was responsible for the present condition. The third case, a single woman, had a fall or injury in a gymnasium ten years before the pelvic examination. Six years previously her cervix uteri had been dilated to relieve dysmenorrhea, and a pelvic peritonitis developed from which she nearly died. The infection subsequent to the injury would be the most logical explanation for the adherent retroversion. The fourth case was a married woman who a few months before had a miscarriage at two and a half months, occasioned according to her history by a fall down stairs. Her chief complaint was exhaustion, although there was some first-day menstrual pain. She had an apical tuberculous lesion and poor cardiac musculature. These

two medical conditions would, no doubt, be more at fault in producing her general weakness than the retrodisplaced uterus found on pelvic examination, and for which she blamed the fall. The fifth case was a married woman who, four years previous to the pelvic examination, during her first year of married life had a miscarriage at three months. Three years later she fell across a chair. Her menstrual history was normal until three months before the examination, when she developed metrorrhagia. She had a bearing-down feeling and complained of pain on defecation. Examination revealed a fissure in ano, marked pain over the appendix, a large cervical polyp, and a retroversion. As polypi are so frequently the result of retained secundines, especially following abortions, the retroversion was much more likely to have been the result of the premature interruption of the pregnancy with the admittedly poor after-care than the minor accident of falling over a chair. In the sixth case the woman fell astride a chair with the development of abscesses, which required incision. This is the history of trauma in a woman whose retrodisplaced uterus was accompanied by pain in the ovaries and metrorrhagia. The history here is too scant to judge what merit the fall might have had in producing the displacement. The seventh patient had a fall fifteen years before the pelvic examination, but the symptoms pointing to the displaced uterus only appeared after a miscarriage a few months previously. The recent miscarriage in this instance is much more likely to have been the cause than the injury sustained so long before. The eighth case, a woman married eight years, had her first pregnancy interrupted, according to her history, by a fall the nature of which is not specified. She dated her chief complaint of pain in the side to a second fall four months before the examination. She had appendicitis, a floating right kidney, and a displaced uterus. While the first fall may have caused the miscarriage, it is just as likely that the uterus was left in a retroverted position after the miscarriage, and that the symptoms of the total pelvic pathology were aggravated enough by the second fall to necessitate a pelvic examination by which the displacement was found. The ninth case, a single woman, dated her trouble, leucorrhea and pelvic discomfort to excessive horseback-riding seven years before the examination. It might be possible that the pelvic viscera and the supporting ligaments would permit a displacement through a long-continued strain as indicated in the history. The tenth case, a single woman, complained of pain along the sciatic nerve, not affected by menstruation, and some irritation of the vulva. The symptoms were stated by the patient to have been apparently started by a fall, and aggravated by another fall. Examination disclosed an anteflexed and retroposed uterus of an infantile type. The condition of the uterus is that most commonly found in cases of congenital retrodisplacement, and it is just as likely that this

was the original condition as that it was caused by the fall. The eleventh case was a single woman who dated her chief complaint of leucorrhea from a fall two years earlier. She had severe menstrual cramps after the fall and pain on the right side of the abdomen. Examination revealed a thickening in the base of the right broad ligament and the uterus halfway over. Here the fall probably had less to do with the uterine condition than the inflammatory condition alongside it. The twelfth case, a single woman, complaining of dysmenorrhea, leucorrhea, and backache from puberty, did not have her symptoms affected for the worse by a fall down three stairs a short time before the examination, and which resulted in a severe sprain of an ankle- and knee-joint.

The thirteenth case, a single woman, likewise complained of dysmenorrhea and backache from puberty eleven years before. She had no increase in the severity of the symptoms as a result of a fall from a carriage five years before the pelvic examination revealed the presence of a retrodisplaced uterus.

It is seen, therefore, from a study of these few cases how small and uncertain extent such injuries as falls and strains can be considered as a cause of uterine displacements. It is true that an occasional case is reported in the literature where a uterus found in perfect position a short time before an injury was sustained has been found retrodisplaced on examination made immediately afterward. The suspicion must arise that some accompanying pelvic lesion existed or an examination would hardly have been sought before the fall.

It should be necessary in a legal action to recover damages to show that the patient had been healthy and physically able, and that the uterus was in a normal anteflexed position before the accident. As has been shown above, some women have apparently perfect health and are physically able, and yet whose displacement may only have been noticed after marriage on account of sterility; it would seem difficult to prove satisfactorily that the uterus could have been in normal position without a previous examination. The nature of the accident would have to be considered as to the manner in which it could produce the retrodisplacement of a previously normal uterus. It is possible to conceive, as above stated, that a partially retroverted uterus could by a hard fall on the back or buttocks be converted into a completely retroverted uterus, but it is equally inconceivable that a fall forward on the face or side could be able to produce any such displacement. Insofar as the subjective symptoms are concerned it is seen that few if any symptoms are produced by a simple retrodisplacement. It should be necessary to have proved that immediately after the accident a retrodisplacement did exist. But although after such an accident a retrodisplacement was discovered, this fact would in itself be no evidence that a displacement had not existed previously, even though no symp-

toms were manifested by it. That retroversion may be caused by trauma is possible, but it is apparent, from the facts stated above, that traumatic retrodisplacement of the uterus is very rare; and that unless it can be shown that the uterus was in normal position just before the accident or injury, it is impossible to prove that the displacement had a traumatic origin.

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CERTAIN UNCLASSIFIED FEVERS: THE TYPHACEÆ (TYPHOID GROUP) AND ENTERICOID OR PARAENTERIC FEVER.

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By unclassified fevers I understand certain forms of infectious fevers which, though frequently met with, and, in part, at least, well known to clinicians in a general way, have not as yet been definitely named. This is due to the fact that often they are passed over as unimportant, and have therefore not been subjected to an exhaustive bacteriological study. Perhaps the main reason why they have not been differentiated is, that our present methods of investigation—bacteriological, chemical, and otherwise—are not far enough advanced to enable us to classify these fevers nosologically.

The fevers under discussion are primarily caused by infective agents, as distinguished from those fevers which are due to disturbances of the function or of metabolism. This latter group may be designated as the fevers of endogenic origin. Menstrual fever may be cited as an example of this type.

The fevers under discussion are also distinct from the fevers of exogenic, chemical origin. Finkelstein's resorption fever after sugar installation in infants is an example of this type. What is generally called gastro-intestinal auto-intoxication is a chapter by itself, the import of which is still *sub judice*. If auto-intoxication causes fever at all it is, in a given case, very difficult to state what part, or how much of the fever, is due to the absorption of the toxic products from the surface of the gastro-intestinal tract, and how much is due to the accompanying bacteremia. What is now popularly called ptomain poisoning, comes under this heading. It is probably nothing more than a gastro-enteritis of bacterial origin. The fevers caused by group A of the paratyphoid bacilli are often accompanied by an acute gastro-enteritis. This is one form of paratyphoid A infection. Both paratyphoid A and B infections, however, may present the complete clinical pictures of typhoid fever. The enteritis of the first form is the result of surface infection. The typhoidal symptoms of the second form are the result of blood-invasion of the paratyphoid bacilli.

Out of the large number of unclassified fevers, I will confine my remarks to a number of those which resemble typhoid fever. Since I have begun to study these cases my attention is not infrequently directed in hospital service toward a form of fever which is brought in, because the patient arouses the suspicion of having a typhoid infection. These cases have the general clinical aspect of that disease. In their future course, they may or may not develop into a genuine case of typhoid fever, as the saying goes. More often, they defervesce in a week or ten days. I am not inclined to think that these cases are abortive cases of typhoid fever. In private practice the occurrence of these typhoid-like fevers are a source of anxiety to the family. A positive answer as to the nature of the illness which is demanded for hygienic and prognostic reasons can often not be given.

The course of this fever resembles that of a mild infection; it comes nearer to the descending curve of the third week of a mild typhoid fever than anything else. Blood cultures are negative. The blood count shows leukopenia or moderate leukocytosis. Eosinophiles are often absent. Relative lymphocytosis may be present or absent. There is no predominating symptom present, pointing to any of the organs. Persistent search for catarrhal symptoms in the respiratory organs is mostly fruitless. In the lack of symptoms—intestinal, respiratory, and otherwise—in the general prostration, the marked enlargement of the spleen—I have palpated the spleen in several instances—in the configuration of the fever curve these fevers strikingly resemble a mild or abortive case of typhoid fever. It must be admitted that these fevers are possibly cases of so-called auto-intoxication. Still, it is difficult to prove them as such, as the decomposition products in the urine,

in the shape of the aromatic bodies, scatol, phenol, and indol, are missing.

Judging by analogy, we are dealing here with a mild bacteremia not unlike a typhoid infection. The infective agent in all probability enters the blood through the portals of the respiratory or intestinal

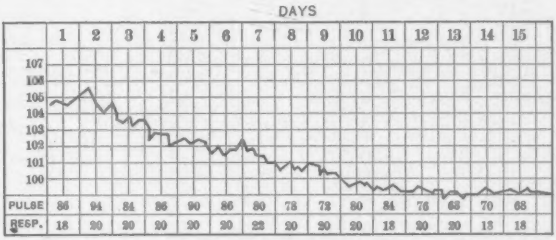

CHART I.—Entericoid or paraenteric fever. Blood count on the third day of the fever: lymphocytes, 28 per cent.; polynuclears, 60 per cent.; large mononuclears, 10 per cent.; eosinophiles, 1.5 per cent. Widal and Diazo negative throughout. Agglutination against six paratyphoid strains negative.

lymphatic system. This can only be proved by positive blood cultures which, so far, have not been realized.

Those of us who practised during the great influenza pandemics of the late eighties and early nineties, observed cases of group-infections of influenza in families, some of which strikingly resembled

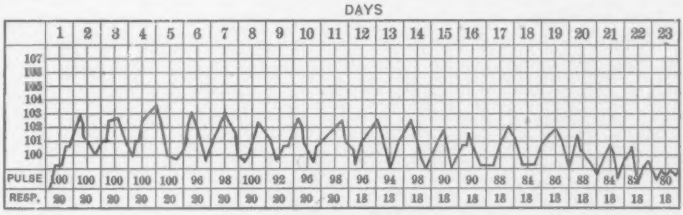

CHART II.—Entericoid or paraenteric fever. Blood count on the second day: reds, 4,328,000; leukocytes, 12,200; small mononuclears, 10 per cent.; large mononuclears, 9.5 per cent.; polymorphonuclears, 79 per cent.; eosinophiles, 1.5 per cent. Blood count on the fifteenth day: reds, 3,853,000; leukocytes, 13,500; small mononuclears, 24.6 per cent.; large mononuclears, 13 per cent.; polymorphonuclears, 59 per cent.; eosinophiles, 3.4 per cent. Widal reaction negative up to 1 : 100. Diazo negative. Agglutination against six paratyphoid strains negative.

typhoid fever. Since that time I observe every year a number of cases of fever, typhoid-like in character, which go under the name of influenza, but which are not caused by the influenza bacillus of Pfeiffer, as proved by negative sputum culture, in appropriate media, but are due to infection with pneumococci or streptococci.

These fevers may start in with catarrhal respiratory signs. If they do not, they are often unmasked late in the disease by resolving into a predominant general bronchitis.

In an interesting contribution by Dr. David Riesman of Philadelphia, discussed by Dr. Hobart Amory Hare,[1] it is proposed to call the fevers allied to the typhoid fevers, entericoid fevers, febris entericoides. I have called them typhocoid or paranteric fevers. Presumably these fevers are caused by the bacteria closely allied to the bacillus of Eberth. Since Schottmüller's description of the paratyphoid groups A and B, a dozen or more observers have added distinct varieties of this group which are known by the names of the discoverers. Typhoid-like fevers may also be caused by the paracolon bacilli. Warren Coleman[2] described a case clinically identical with typhoid fever, inclusive of rose spots, caused by a colon bacillus. Schottmüller[3] recently described an epidemic of herpetic fever in women, which was associated with urinary symptoms. The pus in the (oral) labial herpes contained a pure culture of a colon bacillus.

Someone has said that Escherich's discovery of the colon bacillus was hailed as an unwelcome event in bacteriology, as innumerable questions, serological and otherwise, were raised by the seemingly inexhaustible number of strains of the colon bacillus; the answers to most of these questions have so far been unsatisfactory, especially has this been so as regards the subject under discussion. Perhaps some day will be written the biological history of the ascendency of the colon bacillus into the fixed types of the various forms of typhoid fever.

It might not unjustly be said, that the foregoing observations on the interpretation of these unclassified fevers have, after all, only a theoretical or at most, a purely scientific significance, were it not for the fact, that in a number of instances, I have seen mild fevers of this kind, after a short subsidence, merge into severe cases of typhoid fever. Now there can be no doubt that in these instances these initial febrile movements which are seemingly identical with the entericoid or paraenteric fevers described above, constitute the introductory stage of true typhoid fever. We must assume that after the usual low temperature fluctuations of the incubation stage of typhoid fever is passed, there is a preliminary or initial fever, in these cases of typhoid fever of a week's, ten days, or fortnight's duration. Sometimes this initial fever is apparently nothing else than a primary access in irregular, atypical forms of typhoid fever. The complete *ensemble* of the case then shows a series of such accesses with remissions. It lies in the nature of the case, that the initial stages of typhoid fever have not been subjected to the careful observations of the later stages. In the large

[1] Jour. Amer. Med. Assoc., December 29, 1913, p. 2205.
[2] Amer. Jour. Med. Sci., 1909, cxxxviii, 198.
[3] Beiträge z. Klinik d. Infectionskrankheiten, vol. i, No. 1.

number of cases, at least in hospital practice, the patient does not come under observation before the second or third week of the fever, or even later. I have at present a case under observation, which presented this initial stage. At that time the patient showed a large spleen with a mild febrile movement. Diazo reaction negative. After a short remission, rapid rise of temperature, spleen larger, diazo strongly positive, blood-culture negative. Numerous rose spots. Moderate leukocytosis, eosinophiles constantly present. Widal reaction, taken every few days, absolutely negative. In the sixth week, Widal positive, 1 to 20. It has been negative ever since. Reaction against all available paratyphoid strains negative. Culture of urine and feces negative. Complement-fixation for typhoid fever negative. The steady increase in hemoglobin and eosinophiles and the slow but certain reduction in the size of the spleen in this, the eighth week, seems to prove that complete convalescence has already set in.

From what has been stated it becomes evident that the fevers under discussion will bear close study. In a given case, the question to be decided is, Am I dealing with a case of typhoid fever or not? This is often decided soon enough, when unmistakable clinical evidence is present. The laboratory corroborates the diagnosis sooner or later. If the diagnosis of typhoid fever cannot definitely be made, the situation is a puzzling one. We have seen that there is a class of fevers, clinically resembling typhoid fever, which at present it is hard to classify, and to give a distinctive name. No doubt we are dealing with infections of various kinds. Their true nature will not be determined until they are subjected to an exhaustive biological research.

Furthermore, there is a class of fevers which clinically are unmistakably typhoid fevers, but in which, also, the laboratory proof is inadequate. This opens up the large question of the biology of the typhaceæ. This name has been used by Loeffler[4] to designate the colon, paracolon, paratyphoid, and typhoid groups of bacteria. The same name, I think, may also be used as a collective appellation for the various groups of fevers caused by these typhoidogenetic bacteria. Typhoid fever, a clinical entity, is produced by a variety of infective agents. Some of these have been determined; their biological reactions are well known. Others are still to be isolated. A comprehensive study of the bacteriological relationships of the typhaceæ fevers among themselves, the determination of the appropriate culture media for each variety of bacteria, the amplification of our knowledge of agglutination, complement-fixation, opsonic index and other biological reactions will serve to classify the individual case in the clinic.

For valuable assistance in the laboratory, I am indebted to Drs. Hensel and Garbat.

[4] XIV International Congress for Hygiene and Demography, 1907, and Weber and Haendel, XV International Congress for Hygiene and Demography, 1912.

REVIEWS

A Practical Treatise on Diseases of the Skin. By Oliver S. Ormsby, M.D., Professor and Head of the Department of Skin and Venereal Diseases, Rush Medical College (in Affiliation with the University of Chicago); Dermatologist to the Presbyterian, Children's Memorial, Saint Anthony's, and West Suburban Hospitals, The Home for Destitute Crippled Children, and The Orphan Asylum of the City of Chicago; Member of The American Dermatological Association and of the Congress of American Physicians and Surgeons. Pp. 1168; 303 engravings and 39 plates in colors and monochrome. Philadelphia and New York: Lea & Febiger, 1915.

The writer first gives a detailed account of the anatomy and physiology of the skin, general symptomatology, etiology, pathology, diagnosis, prognosis, and therapeutics. The diseases of the skin, for the purposes of study, are divided into nine classes: hyperemias and inflammations; hemorrhages; hypertrophies, atrophies; pigment anomalies; new growths; neuroses; parasitic affections, subdivided into diseases due to vegetable parasites and diseases due to animal parasites; diseases of the appendages, subdivided into diseases of the sweat glands, sebaceous glands, hair and hair-follicles, nails, and mucous membranes. This classification is practically the same as used by Hyde, with the exception that the term neuroses is substituted for sensory dermatoneuroses and the group "Diseases of the tropics and warm countries exhibiting cutaneous lesions" is omitted.

The writer speaks authoritatively of pellagra; as Secretary of the Illinois Pellagra Commission, he had a considerable opportunity of studying this important disease; several excellent photographs are given. Thirty pages are devoted to the exanthemata which enhances the value of the present volume. The Wassermann and luetin tests are given in detail, including their value in syphilis. The therapeutic indications and the exact method of employing salvarsan and neosalvarsan are presented. The term xanthelasma is used for eyelid xanthoma, as suggested by Pollitzer and adopted by the American Dermatological Association. The classification of syphilis, as suggested by George Henry Fox is mentioned but not employed in the present volume. The important subject of leukemia cutis is given in considerable detail, which is a great

advance over most of the recent works on dermatology. The general subject of trichophytosis is brought up to date by the inclusion of several photographs of plate cultures showing the ringworm fungus. The pathological description of the various dermatoses is fully and clearly given and numerous photomicrographs help in the elucidation of the text. The author has drawn largely from his own collection of photographs, those from the former edition of Hyde's treatise and from his many friends, thereby giving his volume the aspect of an atlas in addition to the valuable reading mater. All of the common and most of the unusual cutaneous affections are depicted in either black and white or color. The book is an important addition to the dermatological field. If any criticism could be offered, the reviewer would state that the present volume is practically a revision of Hyde's *Diseases of the Skin*. A revision which makes the latter volume complete with all of the many advances in the dermatological field. F. C. K.

PATHOGENIC MICROÖRGANISMS: A PRACTICAL MANUAL FOR STUDENTS, PHYSICIANS AND HEALTH OFFICERS. BY WILLIAM H. PARK, M.D., Professor of Bacteriology and Hygiene in the University and Bellevue Hospital Medical College, and Director of the Bureau of Laboratories of the Department of Health, New York City, and ANNA W. WILLIAMS, M.D., Assistant Director of the Bureau of Laboratories, New York City; Consulting Pathologist to the New York Infirmary for Women and Children. New (5th) edition, thoroughly revised. Pp. 684; 210 illustrations and 9 full-page plates. Philadelphia and New York: Lea & Febiger.

THE fifth edition of this valuable manual appears, after a four-year interval, with 18 more pages and 14 more engravings and 9 full-page plates instead of 8. Only one of these, however, is the same in the second edition. Especially noteworthy are Williams' drawings of protozoa and Negri bodies.

Under a new arrangement of material, Part I deals with Principles of Microbiology; Part II, Pathogenic Microörganisms Individually Considered; Part III, Applied Microbiology. This last part, a development of three chapters scattered through the previous editions takes up the relations of milk, water, air, soil, and sewage to disease, bacteriological methods of examination of the same, and practical disinfection and sterilization.

It is pleasant to note the "up-to-date" treatment of trachoma and rabies, Cole's differentiation of four types of pneumococci, and of Mallory's recent studies in pertussis. Noguchi's growth of the rabies organism on artificial cultures is not corroborated; one

regrets that space has not also been found for treatment of Gay and Claypoole's work on *Streptothrices.*

The index is full and conveniently preceded by an author's index. The book is of great value to medical students, both graduate and undergraduate. E. B. K.

TEXT-BOOK OF SURGICAL OPERATIONS ILLUSTRATED BY CLINICAL OBSERVATIONS. FOR PHYSICIANS AND STUDENTS. By PROF. FEDOR KRAUSE, Privy Medical Councillor, Directing Physician Augusta Hospital, Berlin, in association with EMIL HEYMANN, M.D., Chief Physician, Augusta Hospital. Translated and Edited by ALBERT EHRENFRIED, A.B., M.D., F.A.C.S., Assistant Visiting Surgeon, Boston City Hospital; Assistant in Surgery, Harvard Graduate School. Vol., 1; pp., 267; 55 plates having 233 colored illustrations, 61 figures in text. New York: Rebman Company, 1915.

BY being the first to excise the Gasserian ganglion, in 1893, Prof. Fedor Krause ranks with the immortal German surgeons of the nineteenth century who originated operations, and is the worthy successor at the Augusta Hospital of another of this small group of five, Ernst Kuester. In his own words: "The purpose of the book consists in this, that it offers to every properly trained physician a foundation upon which he can independently undertake the operations described. In order to fulfil this purpose in all its details, pictures true to nature explaining the different phases of each operation have been liberally supplied on special plates." And in the words of the translator: "This book is, primarily, a text-book of operative surgery. It approaches its subject in a novel way, by the presentation and discussion of actual cases, which are carefully followed from the beginning, through the operative treatment, to the end-result. These cases illuminate the text and give a touch of practical interest to what might otherwise be a dry discussion. This is, in fact, an application of the case-teaching method to surgery." Perusal of the volume bears out these statements completely.

The twelve chapters cover general surgical technique and operations upon the head. The first four chapters, occupying the first seventy-nine pages, and covering the grounds of preparation for operation, anesthesia, asepsis and after-treatment, might have been omitted with advantage, as they are not germane to the scope of the book, and are so elementary that one who has not already mastered them in the days of his internship had better not attempt to perform the operations that follow. Furthermore, German technique differs in many respects from American, and it seems useless to complicate matters.

A few minor criticisms of details, throughout the book might be made. Most of us would find it very difficult to "tie every spurting vessel" of the scalp. We agree that every accidental wound of the scalp should be considered septic, and explored for injury to the skull. We do not agree that "excellent results may be obtained with scarlet red or fuchsin ointments." Radium should be recommended for hemangioma of the face. The conjunctiva cannot be spoken of as "mucous membrane," for it, as well as the lining of the prepuce and covering of the glans, is modified skin (ectoblast). Unfortunately, the fallacy of referring to lymph nodes as lymph glands is made in this work. In carcinoma of the lip it is advised to ablate cancerous lymph nodes after the extirpation of the lesion. For obvious reasons we consider it better technique to reverse this order. It is easier and less traumatizing to remove the outer wall of the orbit with the Gigli or motor saw than with the chisel. In children the mastoid cells are not developed, but this is not brought out in the book. The suprameatal triangle, the guide to the antrum, should bear MacEwen's name. In Schloffer's method of exposing the sphenoidal sinus and the hypophysis the following direction is given: "After a small sagittal incision was made with a knife in the middle line 56 cm. behind the bony root of the nose." This sentence should continue: "the undertaker should be summoned." Of course, 56 mm. is meant. It is not clear how the frontal nerve can be exposed without cutting through the periosteum of the roof of the orbit, for it lies under cover of that membrane. Blocking of the lingual nerve within the mouth should be performed instead of resection. After excision of the second and third divisions of the fifth nerve, Kanavel's method of plugging the foramina with bone-pegs receives no mention.

The arrangement of the book is ideal in that almost every technical detail is illustrated, leaving nothing to the imagination of the reader. The illustrations are copious—even lavish—and of artistic merit. The translation is so well done that one could scarcely believe the book had been written in another language.

If the remaining volumes fulfil the promises of the first, we would say that the ideal work on operative surgery has appeared at last.

P. G. S., Jr.

Cancer: its Cause and Treatment. By L. Duncan Bulkley, M.D., Senior Physician to the New York Skin and Cancer Hospital. Pp. 230. New York: Paul B. Hoeber, 1915.

Bulkley endeavors to prove in his small volume that the eradication of cancer depends largely, if not wholly, upon proper metabolism. The metabolic process being entirely correct if the character

of the food ingested is restricted to certain articles and the kidneys and bowels are either normal or have an increased activity. The writer states that to prevent the occurrence or recurrence of cancer, it is absolutely necessary to maintain a perfect vegetarian diet, which includes even the exclusion of eggs and milk from the food. The distribution of cancer is governed by the diet; those races indulging largely in meat are very prone to the tumor formation, while those partaking exclusively of a vegetarian or rice diet are comparatively free from the disease.

According to Bulkley, "there have been plenty of good men who knew the disease and have reported favorable results, and even complete disappearance of cancer, under dietetic regimen and proper medication alone, without operative interference of any kind." Several cases of cancer of the breast, with lymphatic gland enlargement, are cited which entirely recovered under vegetarian or rice diet and the free flushing of the intestinal and urinary tracts. The millennium insofar as the cure and prevention of cancer, has come if we all could only obtain the results of the writer of the attractive and readable volume under discussion. F. C. K.

PYELOGRAPHY (PYELO-URETEROGRAPHY). A STUDY OF THE NORMAL AND PATHOLOGICAL ANATOMY OF THE RENAL PELVIS AND URETER. By WILLIAM F. BRAASCH, M.D., Mayo Clinic, Rochester, Minnesota. Containing 296 Pyelograms. Philadelphia and London: W. B. Saunders Company, 1915.

To Braasch more than any man in this country belongs the credit of demonstrating the value of pyelography in the diagnosis of surgical diseases of the kidney. As the result of his large experience and careful observations, he is especially fitted for the preparation of this excellent monograph which takes up every phase of the subject, including an exhaustive survey of the literature. The opening chapters contain a *resume* of the history of pyelography together with the accidents that may follow collargol injection. The author is of the opinion that these ill results are in the majority of instances attributable to faulty technic or improper selection of cases. He states that pyelography has proved of too great value to allow it to be discarded because of an occasional reaction, but it should be employed only with the strictest precautions and by those who are expert in cystoscopic work. Numerous pyelograms are given illustrating the various types of the normal pelvis and ureter. Accompanying these are detailed descriptions, making the chapter of especial value. The succeeding chapters are devoted to deviations from normal as the result of disease. Both mechanical and inflammatory dilatations of the

pelvis are discussed from the standpoints of diagnosis and the types of cases suitable for injections. In cases of renal calculus, pyelography should be employed only when interpretation of the plate is doubtful or when exact localization is desirable. That pyelography is of decided value under such circumstances is nicely shown in numerous plates. The final chapters deal with tumors of the kidney and congenital anomalies in their relation to pelvic distortions, et cetera. We have nothing but praise for this monograph which presents the last word in pyelography. F. E. K.

THE CLINICS OF JOHN B. MURPHY, M.D., at Mercy Hospital, Chicago. Volume IV, Number II (April, 1915). Octavo, 197 pages, 47 illustrations. Philadelphia and London: W. B. Saunders Company, 1915.

THE present issue of *Murphy's Clinics* opens with a diagnostic talk by Dr. Murphy on osteomyelitis. While this is written in Dr. Murphy's best vein, yet but little is added to what has been covered by four talks in previous numbers.

The next case is one of "Bony Lipping of the Right Acetabular Margin and of the Neck of the Femur Following a Metastatic Arthritis—Arthroplasty of the Hip—Cheilotomy." Subscribers to the *Clinics* must have acquired a fair knowledge of this subject from the eight talks on the hip that have appeared in previous issues. The Roentgenogram presents the appearance of the common hypertrophic osteoarthritis, or morbus coxæ. The operation is termed cheilotomy one place and cheilectomy another.

Dr. Rodman's talk on "Carcinoma of the Breast" is very elucidative. His experience with Paget's disease must have been exceptionally extensive to warrant the phrase, "Nearly all the patients with it that I have seen . . ." His interpretation of the pathology, that it is duct cancer with secondary cutaneous involvement, should be emphasized. He states in italics: "*The muscles are removed not because they are involved in the carcinomatous process*, as so many think, *but simply for the reason that a thorough axillary dissection cannot be made with the muscles in situ.*" If this is the only reason, why remove the pectorals at all? Why not reflect them and stitch them back, just as when one deals with the infrahyoid muscles in the removal of a large goitre? Referring to ligation of the superior thoracic artery, Dr. Rodman says: "I have convinced myself by work in the dissecting-room that it is at least a hazardous, if not an unwarranted, procedure." And yet on the very next page, "The superior thoracic, which is about the middle of the upper flap, is seized and ligated."

The fourth case is an inoperable carcinoma of the colon with

diffuse miliary "carcinosis" of the peritoneum. A case of carcinoma of the colon was discussed in a previous issue.

The fifth case is one of epithelioma of the upper lip starting in an old lupus scar, for which excision, with plastic closure, was performed. The sixth case is an intramural fibroid of the uterus. The seventh case is one of hypertrophy of the prostrate, complicated; perineal prostatectomy. Much of the ground was covered in two previous talks, one of which appeared in the October, 1914, number.

The eighth and last case, one of spontaneous massive coagulation of cerebrospinal fluid with xanthochromia, was introduced with a diagnostic "talk" by Dr. Mix. This assumed monographic proportions, covering 52 pages, and leaves one in a quandary how Dr. Murphy found any time left to operate that day. It includes abstracts of 33 cases from the French and German literature, with a complete bibliography at the end. Readers of the *Clinics* are more apt to be bored than entertained by this "talk," unless they be neurologists, but Dr. Murphy sums up the essential points in his ensuing comments, which form the most interesting part of this issue. Two excellent illustrations, one in colors, by Tom Jones, are included here.

Boiling the issue down, the faithful subscriber gets very little "new" material. He only gets 8 topics, whereas previous issues have contained from 12 to 21. It seems far better to maintain the freshness of this publication by issuing it quarterly or even semi-annually, than to be forced to the necessity of repetition and obvious padding, in order to issue it bi-monthly.

BERIBERI. By EDWARD B. VEDDER, A.M., M.D., Captain Medical Corps, U. S. Army. Cartwright Prize for 1913. New York: William Wood & Co.

OF great practical as well as scientific worth this book passes the added distinction of being, for a work of this kind, unusually readable.

The story of beriberi from the earliest times to our own, as presented by the author offers an engrossing tale. It will appeal not only to physicians and scientific men in general, but to anyone who can appreciate the story of a tremendous work well done.

One of its most attractive features is the way in which evidence, offered by opponents to the theory of beriberi to which the author holds, is taken and by careful analysis and the verification or disproof of the facts as stated, is shown to support rather than controvert his belief.

The author proves conclusively, that beriberi is caused by a

dietary deficiency; that it is a lack in various diets rather than a specific poison or infection in them that is at fault.

The correlation of the beriberi of fowls and animals with human beriberi makes possible the experimental proof of beliefs formed from the observation of beriberi in man.

The only criticism, if such it may be called, is that after driving a truth home and clinching it, the author proceeds to clinch it time and again. This may, at times, weary a reader who has grasped the significance of proofs offered and already formed his conviction.

Practically the beriberi question should be in large part a closed one and the ravages of this dread disease in the Orient and elsewhere (for it is shown to be of almost world-wide distribution) should cease. A. A. H.

TEXT-BOOK OF ANATOMY AND PHYSIOLOGY FOR NURSES. By AMY S. POPE, Instructor in the School of Nursing of the Presbyterian Hospital in the City of New York. Pp. 545; 135 illustrations. New York and London: G. P. Putnam's Sons.

To be able to say how much and how little a text-book on anatomy and physiology should offer to nurses is a difficult problem to solve. The author of this volume exhibits a proper estimate upon the relative importance of the various parts of her subject matter, and presents them in an entertaining and impressive style. Some features of the usual nurses anatomy have been omitted; not however with any consequence.

The portion dealing with physiology is well done. It keeps pace with the growing needs of the nurse as teacher of hygiene and sanitation, together with her increasing opportunities in the social service field.

While the book is rather fully illustrated, it is not unfair to say that some of the pictures could be improved; especially so, inasmuch as a lasting portion of the nurse's idea must come from these illustrations. T. G. S.

DISEASES OF BONES AND JOINTS. By LEONARD W. ELY, M.D., Associate Professor of Surgery, Leland Stanford Junior University. Pp. 218; 212 illustrations. New York: Surgery Publishing Company.

THE author shows a commendable effort toward compactness and to follow broad general principles. In the first chapter anatomy, physiology, and pathology are discussed, but throughout the whole book pathology receives prime consideration and is

presented in the light of the most valuable recent contribution to the literature, a considerable bibliography being given. Only 38 pages are devoted to bone diseases and 21 pages to acute joint diseases. The greater part of the book is given up to those chronic affections of joints which are so troublesome to the patient and physician and concerning which there is so much to learn. Brevity and comprehensiveness are attained, chiefly, by restriction to general principle and to the gist of the subject. Instead of having on the top of both opposing pages the title of the book it would be better to have on one the title of the chapter under discussion, particularly as six of the nine chapters do not begin on the page indicated by the list of contents. But this detracts little from the value of the book. T. T. T.

DENTAL DISEASES IN RELATION TO PUBLIC HEALTH. By J. SIM WALLACE, D.Sc., M.D., L.D.S., Formerly Dental Surgeon and Lecturer on Dental Surgery, London Hospital. Vol. 8., pp. 90. London: Office of the Dental Record.

BESIDE directing attention to the great prevalence of dental diseases, as well as the seriousness of infections in various parts of the body with the tissues about the teeth as the original foci, the author directs attention to the inter-relationship of food habit and dental caries. He draws attention to the value of a knowledge of the physiology of oral hygiene, especially for medical students, and gives a short but comprehensive treatise upon the same. In closing he describes the results of dental diseases upon the development of children. C. P. S.

AIDS TO DENTAL ANATOMY AND PHYSIOLOGY. By ARTHUR S. UNDERWOOD, M.R.C.S., L.D.S., late Professor of Dental Surgery at King's College, London; Member of the Board of Examiners in Dental Surgery, Royal College of Surgeons of England; Lecturer in Dental Anatomy and Physiology at the Dental Hospital of London. Third edition. Pp. 136. New York: William Wood & Co.

WHILE this little book is concise, it must not be regarded in any sense as a quiz compend or as dealing with essentials only. In fact, it covers thoroughly the whole subject of development, histology, and gross anatomy of the human teeth, together with an insight into comparative dental anatomy. Some of the views expressed by the author upon certain points have not met with general acceptance, notably the alleged demonstration by Mummery

of nerve fibers in the dentine. In an appendix is contained Mummery's communication to the Royal Society, which represents the most recent original work upon calcification of dentine and enamel. A few illustrations would have greatly enhanced the value of the book. R. H. I.

PRINCIPLES AND PRACTICE OF HYDROTHERAPY. By GEORGE KNAPP ABBOTT, A.B., M.D., Dean and Professor of Physiologic Therapy and Practice of Medicine in the College of Medical Evangelists, Loma Linda, Cal. Second Edition. Pp. 510; 127 illustrations. Loma Linda, Cal.: The College Press.

GREAT care has been exercised to make this work thoroughly practical, and while explicitly stating the beliefs and explaining the practices of the most advanced hydrotherapists, the book will surely prove acceptable to the most conservative, and presents in an attractive form, much that will be new to the general practitioner.

This work is a concise treatise on the subject which will give the practitioner as well as the hydrotherapist, in few words, systematically arranged and well illustrated, the key to the successful application of these physiological measures. M. J. W.

THE FECES OF CHILDREN AND ADULTS. THEIR EXAMINATION AND DIAGNOSTIC SIGNIFICANCE, WITH INDICATIONS FOR TREATMENT. By P. S. CAMMIDGE, M.D. (London). Pp. 516; 13 full-page plates, 7 of which are colored, and 96 illustrations. New York: William Wood & Co.

THIS work comprises a very complete and thorough exposition of the laboratory examinations of feces, normal and pathological, and all that they may contain. Of particular practical use are the chapters on the diagnostic value of examinations of the feces, in which the fecal findings in a variety of diseases are set forth, and the appendix, which contains a large number of diet lists for gastro-intestinal affections, advocated by various authorities. Another chapter deals with indications for treatment, including a short description of the caloric method of estimating the value of diets, the dietary indications in certain affections, the use of drugs, vaccines, etc. In the main, the advice conforms to orthodox teaching, but the section devoted to infant feeding is far too didactic and condensed to be of much practical use. To attempt to indicate briefly the royal road to success in infant feeding is but to attempt the impossible. To practitioners and students who desire practical as well as technical aid in treatment and diagnosis, the book makes a special appeal. J. C. G.

MECHANICAL VIBRATION. ITS PHYSIOLOGICAL APPLICATION IN THERAPEUTICS. By M. L. H. SNOW, M.D., Professor of Mechanical Vibration Therapy in the New York School of Physical Therapeutics, etc. New York: The Scientific Authors' Publishing Co.

SNOW'S book deals first with the "development of mechanical vibrations" in which in an interesting fashion he begins with the early records and merges through massage principles into his own topic. He devotes but little to vibration apparatus *per se*. Systems of vibration therapy receive brief mention. Method of application is given special emphasis. General physiological effects are accorded prominence, as are also the principles and effects of mechanical vibration in diagnosis. Influences upon the heart, vascular, ductless gland, lymphatic, respiratory, muscular, nervous, and digestive systems are separately discussed. The theme is an admixture of advanced and elementary facts. In the hands of the younger student of the subject, provided his purpose is to place the principles in a worthy position in therapeutics, the book must be of value. Frequent reference is made to persons as authorities in whom the medical profession as yet has not imposed much trust. There is a trend of suggestion throughout the context which leads the reader to think that its author tends to regard his principle as an independent art in therapeutics. However, the work suggests a vast amount of labor, study and application to principles therein discussed; it will probably help many an honest student of this special theme, and should find its proper level in medical literature.

W. J. M.

SCIATICA. A FRESH STUDY. By WILLIAM BRUCE, M.A., LL.D., M.D., DINGWELL, N.B. Pp. 175; 17 plates. New York: William Wood & Company.

THE hypothesis of Bruce who has observed more than a thousand cases is "that the true cause of sciatica is trouble in the hip-joint." He endeavors to discredit Gowers, though the latter states that senile rheumatic inflammation of the hip-joint is a common cause of sciatica, but maintains that the disease in the nerve is essentially a neuritis and as a rule has attacked the muscular and fibrous tissues first. "Granting the presence of this fibrositis" Bruce contends, "it is not easy to see how the condition is likely to spread to the nerve." The inflammation passes along the white fibrous tissue which extends practically throughout the body. As to an actual neuritis in the sciatic nerve, which Bruce doubts, the Danish surgeon, Pars, who stretched the nerve a number of times, found in at least half of the cases that the nerve was abnormally red.

We see no reference to the masterful article contributed by Professor Karl Petrén in 1909. The differentiation there is made between sciatica due to hip-joint trouble and that of other origins.

N. S. Y.

AIDS TO PRACTICAL PHARMACY. By A. CAMPBELL STARK, M.B., B.S. (Lond), L.S.A. (Eng.) Ph. C., University Medallist and Exhibitioner in Materia Medica, St. George's Hospital, Medical School, etc. Second edition; pp. 165. New York: William Wood & Company.

THIS work, based on the British Pharmacopœia, presents in compact form the important facts concerning the different drugs. Its strongest appeal would be to the pharmacist and after him, probably, to the dispensing physician.

S. J. R.

RENAL DIAGNOSIS IN MEDICINE AND SURGERY. By DR. VICTOR BLUM, Tutor in Urology at the University of Vienna. English Translation by WILFRED B. CHRISTOPHERSON. Pp. 142. New York: William Wood & Co.

THE immense progress made in renal surgery in the past few years is largely due to advances in our methods of determination of kidney function. It is well recognized that the knowledge derived from these functional tests is essential for the proper management of both surgical and medical conditions of the kidney.

The book begins with a consideration of the particular function of each portion of the kidney as established by experiment. The various methods of determination of renal function are then described in detail. Finally the author takes up the application of the various tests to particular lesions of the kidney. In the author's opinion the following tests afford the most valuable information as to the functioning powers of the kidneys: Cryoscopy of the blood and urine, the indigo-carmine test, experimental polyuria, estimation of urea, and diuretic experiments. He apparently does not measure the percentage of indigo carmine excreted, but only notes the time of onset of excretion of the drug, which he prefers to phenol-sulphonephthalein. The use of the various tests is illustrated by many instructive cases of diseased conditions of the kidney and ureters. The literature of the subject is fully reviewed, and the work of a few Americans in this field has been given due recognition.

R. H. I.

EPIDEMIC INFANTILE PARALYSIS (HEINE-MEDIN DISEASE). By PROFESSOR PAUL H. ROEMER, Principal of the Institute of Hygiene and Experimental Medicine of Marburg. Translated by H. RIDLEY PRENTICE, M.D., B.S. (Lond.), M.R.C.P.; Late Resident Medical Officer to the National Hospital for the Paralyzed and Epileptic, Queen Square. Pp. 208; 57 illustrations. New York: William Wood & Co.

THIS is a very good translation of Professor Römer's book on *Epidemic Infantile Paralysis*. The basis of this work was the recent epidemic in Marburg which led the author to investigate this disease from the experimental stand-point. The results of his studies have been published elsewhere and finally resulted in this work which is an excellent presentation of the present experimental, pathological, and clinical knowledge of the disease. There is nothing new in the conclusions simply because we have not as yet reached that stage in which conclusions can be arrived at. This book is along the same line as the very excellent book on the same subject by Professor Wickman. T. H. W.

THE PSYCHOPATHOLOGY OF HYSTERIA. By CHARLES D. FOX, M.D. Pp. 437. Boston: Gorham Press.

THIS book is largely made up of the elucidation of symptoms of hysteria from the standpoint of the French and Boston schools. The Freudian points of view are only mentioned, but are not especially considered. The author has carefully presented the subject and made extensive use of the literature, and if one wishes a careful presentation of symptoms of hysteria, this book fulfills that need. T. H. W.

AMBIDEXTERITY AND MENTAL CULTURE. By H. MACNAUGHTON JONES. Pp. 102; 23 illustrations. New York: Rebman Company.

THIS important matter is discussed in a small popular edition. Medical men and teachers do not always appreciate the value of being able to use both hands, for, as is well known, the left side of the brain, because of the preponderant right-handedness of individuals, is much more developed than the right. This should not be, for we should not have a silent area of the brain. In this book the plea is made for the development of both hands in all matters pertaining to them. Dr. Montessori's method is touched upon. This book should be in the hands of all teachers. T. H. W.

PROGRESS

OF

MEDICAL SCIENCE

MEDICINE

UNDER THE CHARGE OF

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Salvarsannatrium.—WECHSELMANN (*München. med. Wchnschr.*, 1915, lxii, 177) publishes his experiences with about twelve thousand injections of Ehrlich's newest preparation, salvarsannatrium or salvarsan-sodium. This substance possesses all the advantages of salvarsan and neosalvarsan. It is very soluble in water and on exposure to air rapidly becomes toxic. Wechselmann has used the new preparation in doses of 0.3 to 0.45 gm. and has had no reactions following its use in ambulatory and hospital patients. Only twice has he noted morbilliform eruptions. Such doses may be given twice a week and in recent cases, after total dosage of 4 to 6 gm., the clinical symptoms have practically always cleared up, Wassermann reaction has become negative in the serum, and in about 93 per cent. of the cases, the spinal fluid has become negative. The method which Wechselmann has used in giving salvarsannatrium is as follows: The drug is dissolved in 0.4 per cent. sodium chloride solution in proportion of 1 to 100. The salt solution must be prepared from freshly distilled water and chemically pure sodium chloride and is sterilized by boiling in Erlenmeyer flasks. The drug is not added till the solution has cooled. The solution is then filtered through absorbent cotton (Verbandwatte) which has been sterilized by boiling in 0.4 per cent. sodium chloride solution. The flasks, etc., are sterilized by heating to 120° C. In a vast majority of cases, the author has given the drug intravenously.

On the Treatment of Typhoid Fever with Typhoid Vaccine.—H. EGGRETH (*Wien. klin. Wchnschr.*, 1915, xxviii, 209) reports the results of forty-eight cases of typhoid fever treated with Besredka's typhoid vaccine, given according to the method of Kraus. First, a subcutaneous

injection of vaccine was given. Only a slight local reaction was obtained. Then 0.5 to 1 c.c. of vaccine was given intravenously. Each of the forty-eight patients received only one injection. In thirty-eight cases the result was striking, in eight there was little effect; two patients died. In the thirty-eight cases, the injection was followed almost immediately by slight chill and rise of temperature of 1° to 1½° C. The temperature remained at this higher level, to fall by crisis to normal after six to ten hours. Often there was marked sweating with the crisis. There was never any evidence of cardiac collapse; occasionally there was nausea. In addition to the fall in temperature, there was often improvement in the cerebral symptoms, such as headache, vertigo, stupor, etc. In general, it seemed that the patients who were treated in the first and second weeks of the disease and in whom there were no complications, reacted best. Thirty-four of the thirty-eight cases remained afebrile. In one case, the temperature rose the day after the crisis. In the remaining three cases, the temperature rose on the twelfth, fourteenth and sixteenth day, due to parotitis, osteoperiosteitis and endocarditis respectively; all recovered. The second group of eight cases consisted of patients in the fourth and fifth week of typhoid who were suffering with bronchitis, broncho- or pleuropneumonia. In these there was no critical fall of temperature. All of them recovered, however. In the two fatal cases, death followed about three hours after the intravenous injection. One patient was dyspneic, cyanotic and had râles and dulness in the left back. Autopsy showed, in addition to the usual changes of typhoid fever, a beginning pneumonia, some clear fluid in the pericardium, etc. In the second case, the patient was anemic and fresh blood was found in the ileum. The patients were treated in a military reserve hospital. The diagnosis was confirmed in all cases by positive Widal and diazo reactions. Blood cultures apparently could not be made.

On a New Method of Treatment of Tuberculous Meningitis.—J. BACIGALUPO (*München. med. Wchnschr.*, 1915, lxii, 222) reports his observation in three cases of tuberculous meningitis in children, who were treated with old tuberculin intradurally. In the first case treated, the child had general miliary tuberculosis; there was some betterment of nervous symptoms following the injection, but three days later the child died. In two other cases, in which the diagnosis was confirmed by the finding of tubercle bacilli in the spinal fluid, complete recovery followed within twenty days after three and two injections, respectively. In all the cases following the injection, instead of the expected rise, there was a fall of about 1° C. in temperature. The author suggests an initial dose of 1 mg. old tuberculin. As a vehicle for the tuberculin, he recommends cerebrospinal fluid. Details of the cases are not given. This is unfortunate since the results which the author claims for his treatment are so important that full records of his observations would seem to be desirable. (The briefness of the present report in spite of the favorable results reported would seem to make it advisable to proceed with extreme caution before repeating this work. The number of observations which the author reports is too small to have determined the safety of the treatment or the dosage of tuberculin, it would seem.)

A Case of Balantidiosis Treated with Emetin.—R. AXTER-HASENFELD (*München. med. Wchnschr.*, 1915, lxii, 152) reports a case of balantidiosis treated with emetin. For four months, the patient, a woman, aged sixty years, had suffered with a severe diarrhea. She had been given various remedies, she said, without result. There were as many as twelve watery stools daily, containing pus and blood. The patient was weak and emaciated. On physical examination, the internal ternal organs were normal, except the colon. The stools showed Balantidium coli, as many as ten in a field, actively motile. The author administered uzara at first with slight improvement. The patient, however, was still having about eight stools a day. Then he gave 0.03 gm. of emetin hypodermically. In the following twenty-four hours, the patient had only one stool. The same dose was repeated daily until eight doses had been given. The consistency of the stools became firmer, the pus disappeared. After the third injection, the balantidia could no longer be found. The patient was permanently relieved. As balantidiosis is rare in the author's practice, and as the result of emetin treatment was so brilliant, the case is reported in the hope that others may determine whether the drug is a specific in this infection.

The Extent of Protein Digestion in the Presence of Hydrochloric Acid Deficit.—At the suggestion of Prof. Krehl, L. PEL (*Deutsch. Arch. f. klin. Med.*, cxii, 369) has attempted to determine whether the hydrochloric acid deficit sometimes observed after test breakfasts or test meals necessarily means extended cleavage of protein. For the determination of free hydrochloric acid and hydrochloric acid deficit he has employed Günzburg's reagent as indicator. The total acidity has been estimated with litmus paper. The total chlorides were estimated by the method of Lüttke and Martius. An approximation of the extent of proteolysis has been arrived at by determining total nitrogen (Kjeldahl) and amino-nitrogen by the method of Van Slyke. All the values have been calculated on the basis of 100 c.c. gastric juice and also on the basis of 100 gram nitrogen. The acidity has been expressed in cubic centimeters of tenth normal NaOH, the nitrogen in cubic centimeters of tenth normal NH_3. The binding or uniting power (Bindungsvermogen) has been calculated; if free HCl is present this represents the difference between total HCl and free HCl, while with a deficit it is the sum of the deficit and the total HCl. The author has made numerous observations on the filtrates from test breakfasts and test meals. His general conclusions are as follows: (1) The amino-nitrogen, measured by Van Slyke's method, is generally higher relatively after a test dinner than after a test breakfast. (2) The amino-nitrogen, as compared with the total nitrogen, is increased in some cases with hydrochloric acid deficit, not in others. For example, the author found 9 per cent. amino-nitrogen with a deficit of 119 in one case, 14 per cent. amino-nitrogen with free HCl of 68 in another. (3) The HCl-binding power and the amino-nitrogen content, given a like quantity of total N, do not necessarily run parallel, though in some cases one does find high binding power and high amino-nitrogen combined. Extended cleavage of protein is, therefore, not the only reason for high HCl-binding power. Rather it must be supposed that the special nature of the undigested or slightly digested proteins is

responsible in many cases. (4) The HCl-binding power is increased in some cases of deficit not in others. It is practically never sufficiently increased to account for the deficit alone. (5) Among the causative factors in the production of a deficit the most important is an acid secretion inadequate for the amount of nitrogenous bodies present. Differences in the degree of cleavage of the proteins is of secondary importance. Thus in two cases with practically the same HCl-binding power and the same degree of cleavage the free acid was 68 in the one with a deficit of 24 in the other. (6) Thus there are two kinds of deficit, the one with normal protein digestion the other with abnormally extensive hydrolysis of the portein. So far Pel has been able to discover no differential diagnostic value through determining which of these is present.

Nucleinic Acid in Blood Diseases.—W. KONNECKE (*Deutsch. Arch. f. klin. Med.*, 1914, cxv, 177) has undertaken the study of experimental leukocytoses in primary blood diseases, as the results recorded in literature have to do almost entirely with the reaction obtained in normal individuals or those whose blood has been only secondarily affected. Of the various substances employed to produce a leukocytosis, Könnecke found sodium nucleinate given intramuscularly was the most suitable. It was found that the effects of the sodium nucleinate varied according to the functional ability of the bone marrow. Thus, a normal bone marrow whose cells mature more rapidly under the action of nuclein sends a larger number of ripe cells into the blood stream; the result is a moderate leukocytosis. The bone marrow in chlorosis and many secondary anemias (post-hemorrhagic, for example) is hypersensitive, the result being a more marked leukocytosis. In pernicious anemia and many forms of secondary anemia, on the other hand, the marrow was less sensitive than normal, or entirely insensitive to nuclein. In other words, the leukocytosis was slight or entirely lacking. In lymphatic leukemia only the myeloid system reacts. Severe cases of myeloid leukemia show no reaction to nuclein. In mild cases there is a decrease in the total white count following the first injection, due, Könnecke says, to lessening in the number of immature cells. After repeated injections, a leukocytosis may supervene, but if the injections are long continued, the organism becomes accustomed to the irritant and fails to react. The result of the reaction to sodium nucleinate permits one to draw certain conclusions as to the functional ability of the bone marrow, Könnecke says, which may be of value both in diagnosis and prognosis.

A Study of the Kidney Function in Congenital Cystic Kidney.—W. H. VEIL (*Deutsch. Arch. f. klin. Med.*, 1914, cxv, 156) has had the unusual opportunity of studying carefully three cases of congenital cystic kidney diagnosed clinically. His attention was directed especially to the examination of the functional capacity of the kidneys. In all three cases there were bilateral, palpable, polycystic renal tumors. In all of the cases the results of the functional study was the same. Veil found a marked decrease in the ability of the kidney to secrete a concentrated urine, though the diluting power was retained. This inability to concentrate was shown by the passage of normal quantities

of urine when the patient was on a diet poor in salt and nitrogen, with polyuria when the usual mixed diet was given. Otherwise there was no diminution in the ability of the kidneys to secrete nitrogen, sodium chloride and water, but for substances foreign to the body (milk-sugar, potassium iodide and phenolsulphonephthalein) there was a moderate delay in excretion. The finding of traces of albumin in the urine without morphological elements was constant. There was a moderate increase in blood-pressure amounting to 235 to 240 cm. water (v. Recklinghausen). The study of the blood in these cases revealed normal concentration, osmotic pressure, and rest nitrogen.

SURGERY

UNDER THE CHARGE OF

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Complete Fracture of the Lower Third of the Radius in Childhood, with Green-stick Fracture of the Ulna.—SKILLERN (*Annals Surgery*, 1915, lxi, 209) says that there is a fracture of the lower third of the radius and ulna peculiar to childhood, which constitutes about 13 per cent. of fracture of the forearm. This fracture commonly occurs before the age of puberty, is most frequently encountered during the summer months, and is caused usually by the effects of gravity plus momentum. It is characterized by complete fracture of the radius with dorsal and lateral displacement of the lower fragment and by incomplete green-stick fracture of the inner half of the ulna, usually, at a higher level, the outer half remaining intact and maintaining the deformity of the ulna, which is a bowing of the lower fragment toward the radial side and which in turn, maintains the displacement of the distal fragment of the radius. In reducing the displacement the aim must be to convert the incomplete green-stick into a complete fracture by forcibly rupturing the still intact outer fibers, thereby enabling restoration of alignment of the distal fragment of the ulna with that of the axis of the bone, the distal fragment of the radius coincidently shifting itself automatically into position. The criterion of reduction is the restoration of the normal alignment of the inner border of the ulna. Fracture of the lower third of both bones and of the radius alone comprise 70 per cent. of fractures of the forearm in childhood. The site of the fracture and its variety may often be predicted by a knowledge of the history and mechanism of the fall. Injuries to

epiphyses, whether strain, sprain, or disjunction should be recognized and treated as fractures because of their importance in the growth of the bones and because epiphyseal injuries often predetermine infections, typically tuberculous. Diagnosis may be established clinically by the mechanism and "wincing" tenderness. If deformity exist it is unjustifiable to elicit further signs of fracture. Roentgenograms are of corroborative value, but by no means the final arbiters. Their chief value is in showing the degree of deformity and its presence after reduction. Owing to the delicacy of the radius and ulna in childhood fracture is the rule, while contusion and sprain are the exceptions. Treatment is begun by the administration of an anesthetic if deformity exist. Otherwise a carefully prepared and padded splint (or splints) is applied firmly and without undue pressure. Roentgen-ray control of reduction is important. Massage and passive motion are adapted to the individual case. The splints must be removed as soon as there is firm union. Operation is indicated only when conservative treatment is admittedly a failure. It will seldom be necessary. The inlay method of Albee should be used instead of an array of metal fixtures.

Ureteral Calculi; Special Means of Diagnosis and Newer Methods of Intravesical Treatment.—GERAGHTY and HINMAN (*Surg., Gynec. and Obst.*, 1915, xx, 515) base their observations on 67 cases from the urological clinic of the Johns Hopkins Hospital. They say that the symptoms of ureteral calculus are not diagnostic and are insufficient to definitely determine either its presence or position except in rare instances. While radiography is the simplest and probably the most valuable single diagnostic method for the detection of ureteral calculi, even in the most expert hands, a surprisingly large percentage (22.4 per cent.) may be undetected by it. This large percentage of failures demands the employment of supplementary methods before excluding stone with any degree of positiveness. By means of collargol ureterograms a calculus occasionally will be shown which the simple Roentgen-ray failed to reveal. The employment of the wax-tipped catheter is by far the most accurate method for the detection of ureteral calculi, and this method should be in more general use. In 6 out of 30 cases of ureteral calculi (20 per cent.) seen in the last two years, it has located a stone where repeated roentgenographs were uniformly negative. Owing to the great frequency of extra-ureteral shadows in the region of the pelvic portion of the ureter, diagnosis of ureteral stones in this region cannot be accepted without confirmatory information. A considerable number of stones which enter the ureter pass spontaneously, and the discovery of a small calculus is not always an indication for immediate operative interference. Unless the stone is blocking completely or producing repeated and violent colic, simple and manipulative methods should first be employed, For calculi beyond the juxtavesical portion, displacement with the ureteral catheter, injection of oil or the securing of relaxation of the ureteral wall by using the thermocatheter may, in certain cases, result in the expulsion of the stone. When the stone is in the vesical portion of the ureter, cystoscopic procedures should usually be successful. A study of these cases, as well as different series reported in the literature, shows that a considerable portion (14.3 per cent., Geraghty and Hinman; 17 per cent. of

204 cases, Jeanbrau) of ureteral calculi are arrested in the intramural portion of the ureter—a portion which can be readily reached by cystoscopic methods. These methods, therefore, have an increasing field of usefulness.

Periosteal Regeneration of Bone.—SMITH (*Surg., Gynec. and Obst.*, 1915, xx, 547) says the following conclusions are drawn from considerable experimentation carried on at several different institutions, some under very adverse conditions and others under favorable circumstances. The results obtained were absolutely contradictory to each other. This clearly demonstrates that the cellular elements of the stripped periosteum are dependent upon a varying personal factor. It is possible at the present time to vary the end results according to certain technique; the periosteum stripped quickly and with a sharp periosteotome will produce bone in a greater percentage of cases if young animals are used than if fully developed adult animals are employed. Likewise a greater percentage of positive results will be obtained with periosteum which is stripped slowly and with an elevating action of the periosteotome than when the periosteum is quickly torn loose from the compact bone. A very large percentage of positive results can be obtained by using very young animals and small strips of periosteum. Fibrin is a very active stimulant to osteoblastic activity. In the clinical utilization of these facts, many important factors must be taken into consideration with respect to the end results desired; *i. e.*, stage of bone development; care with which the subperiosteal resection is performed; ample allowance should be made for satisfactory conditions suitable to fibrin formation and a generous supply of blood to the part provided for.

The Nervous System and Abdominal Affections.—THIES (*Mitt. a. d. Grenz. geb. d. Med. u. Chir.*, 1915, xxvii, 415) says that in diseases of the intestinal tract one often observes enlargement or diminution and usually a difference in the size of the pupils, or in the opening between the eyelids. The further oralwards the disease in the intestine, the less frequently is the difference in the pupils or eyelids found, and the further rectalwards the disease, the more frequently. These eye symptoms are found with especial frequency in diseases of the organs supplied by the sacral-autonomous nerves, as in the large bowel, the genital organs and the urinary bladder. The difference in the pupils is found more frequently than in the opening of tbe eyelids, especially in diseases of the upper intestinal tract. A difference in the pupils or opening of the eyelids is only rarely found in affections of the kidneys. It is likewise usually absent in affections of the gall bladder without participation of the large bowel. The difference in the pupils or opening of the eyelids disappears, as a rule, after the removal of the local abdominal focus of disease or it is diminished. Occasionally one finds later a reverse difference.

Management of the Convalescent Stage of Hip Disease.—PACKARD (*Amer. Jour. Orthop. Surg.*, 1915, xii, 666) says that he has seen many cases of hip disease in the past year, where the treatment had been discontinued while the patient was in the convalescent stage. These

cases were free from pain, but the limbs were generally flexed and adducted, and in many instances the lameness was increasing, motion was present in some case but generally absent. From his experience he concludes that: Many cases of hip disease are discharged as cured while the disease is still in progress. Great care must be exercised in determining the joint condition, and protection should be continued as long as indications of the disease are present. Repeated Roentgen-ray pictures must be taken as an additional guide for treatment. The deformity of flexion and adduction should be prevented during treatment, but if present, corrected without trauma to the joint. If for any reason there is the slightest evidence of a relapse after the treatment has been discontinued, immediate protection of the joint is demanded. To obtain the best result one should not be content with methods which demand the least time, or nature's cure supplemented by osteotomy, but should always utilize the means that best meet the indications, regardless of the expenditure of the surgeon's time.

The Futility of Arterio-anastomosis in the Treatment of Impending Gangrene of the Lower Extremity.—STETTIN (*Surg., Gynec. and Obst.*, 1915, xx, 381) did a series of eighteen experiments, his aim being to find some way of graphically recording the amount of the arterial circulation possible through venous channels and he called upon the Roentgen rays as an aid. He used lower extremities, freshly amputated, in cases of gangrene from arteriosclerosis or other arterial disease and variously injected these with liquids impenetrable to the Roentgen rays. He says that the arterial circulation to the periphery, even in very advanced arterial disease, is in every respect better and easier than the retrograde venous circulation, mainly because of the obstruction offered by the valves and the short circuiting of the blood through anastomoses of neighboring venous collaterals. The operation is dangerous and the results have been most unsatisfactory, except in a small percentage of cases. The few so-called successful results have been obtained probably more in spite of than because of the operation, inasmuch as various factors play a role in the improvement in these cases, as improvement has been recorded after definite closure of the anastomosis, and as failure has occurred with perfect patency of the arteriovenous fistula. Even if the anastomosis functionates, which it rarely does, there is no possibility of circulatory improvement, but rather quite the reverse. The term "reversal of the circulation," at least so far as clinical cases are concerned, is absurd. Even if the usefulness of the operation were proved beyond question, the possible indications would be restricted to an unappreciable minimum. Stettin, therefore feels that the scepticism of Lejars, Lenormant, and Wettstein is a trifle too mild. Even Coenen is not quite emphatic enough. Stettin rather agrees with Guthrie, who, although having once claimed to have shown with Carrel the possibility of reversal of the circulation in the limb of a dog, deplores the fact that arteriovenous anastomosis should have been applied to the human being for circulatory disturbances of the lower extremity and prophesies its failure; for he, Stettin, believes that it is very questionable if the operation is ever justified. He believes that this procedure should be entirely eliminated from our surgical repertoire.

THERAPEUTICS

UNDER THE CHARGE OF

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The Effect of Lumbar Puncture in Delirium Tremens.—STEINEBACH (*Deutsch. med. Wchnschr.*, 1915, xli, 369) says that the cerebral pressure is increased absolutely in most cases of delirium tremens and probably is relatively increased in all. He found the cerebrospinal fluid under considerable pressure in one patient who showed inactive pupils to light—and the delirium subsided immediately after a lumbar puncture. He says that Schott-Müller has claimed that in acute alcoholic intoxication the cerebrospinal fluid is always under increased pressure and that alcohol is present in the fluid. Acting upon these observations Steinebach has systematically applied lumbar puncture for the treatment of delirium tremens. His results have confirmed his impression that the abnormally high pressure is responsible for the symptoms of delirium. He does not believe that the alcohol content of the spinal fluid is directly responsible for the delirium but is inclined to attribute the symptoms to a combination of high cerebral pressure, with a secondary poison generated by the alcoholic intoxication. The relief of symptoms following lumbar puncture is due not only to a regulation of the pressure but also to the renewal of a certain amount of poison accumulated in the cerebrospinal fluid under tension.

Kaolin and Blood Charcoal in the Treatment of Diarrhea Processes.—WOLFF and EISNER (*Therap. d. Gegenw.*, 1915, lvi, 92) says that bolus alba (Kaolin) which has been recommended for years as the best treatment for cholera has been proved most efficient by the experiences in the present war. It seems to act by absorbing the toxins and mechanically engulfing the bacteria and carrying them away with it. Blood charcoal acts very similarly and the two can be used in combination. He gives details of twenty-five cases of various diarrheal diseases including dysentery and typhoid fever, showing the almost immediate arrest of the diarrhea after the use of kaolin and charcoal. The kaolin and charcoal can be given in oatmeal gruel, care being taken to prevent them from settling to the bottom by constant stirring. This method of treatment was also used with apparent success in some healthy bacillus carriers, no bacilli being found in their stools after treatment. The author adds that no treatment is so simple nor is it easy to imagine anything more harmless.

The Treatment of Typhoid Fever with Dead Cultures of Typhoid Bacilli.—GOLDSHEIDER and AUST (*Deutsch. med. Wchnschr.*, 1915, xli, 361) report a series of fifty-seven typhoid patients treated with good results by vaccine made with killed cultures of typhoid bacilli. They found that, after a preliminary increase in the fever which at times

cases were free from pain, but the limbs were generally flexed and adducted, and in many instances the lameness was increasing, motion was present in some case but generally absent. From his experience he concludes that: Many cases of hip disease are discharged as cured while the disease is still in progress. Great care must be exercised in determining the joint condition, and protection should be continued as long as indications of the disease are present. Repeated Roentgen-ray pictures must be taken as an additional guide for treatment. The deformity of flexion and adduction should be prevented during treatment, but if present, corrected without trauma to the joint. If for any reason there is the slightest evidence of a relapse after the treatment has been discontinued, immediate protection of the joint is demanded. To obtain the best result one should not be content with methods which demand the least time, or nature's cure supplemented by osteotomy, but should always utilize the means that best meet the indications, regardless of the expenditure of the surgeon's time.

The Futility of Arterio-anastomosis in the Treatment of Impending Gangrene of the Lower Extremity.—Stettin (*Surg., Gynec. and Obst.*, 1915, xx, 381) did a series of eighteen experiments, his aim being to find some way of graphically recording the amount of the arterial circulation possible through venous channels and he called upon the Roentgen rays as an aid. He used lower extremities, freshly amputated, in cases of gangrene from arteriosclerosis or other arterial disease and variously injected these with liquids impenetrable to the Roentgen rays. He says that the arterial circulation to the periphery, even in very advanced arterial disease, is in every respect better and easier than the retrograde venous circulation, mainly because of the obstruction offered by the valves and the short circuiting of the blood through anastomoses of neighboring venous collaterals. The operation is dangerous and the results have been most unsatisfactory, except in a small percentage of cases. The few so-called successful results have been obtained probably more in spite of than because of the operation, inasmuch as various factors play a role in the improvement in these cases, as improvement has been recorded after definite closure of the anastomosis, and as failure has occurred with perfect patency of the arteriovenous fistula. Even if the anastomosis functionates, which it rarely does, there is no possibility of circulatory improvement, but rather quite the reverse. The term "reversal of the circulation," at least so far as clinical cases are concerned, is absurd. Even if the usefulness of the operation were proved beyond question, the possible indications would be restricted to an unappreciable minimum. Stettin, therefore feels that the scepticism of Lejars, Lenormant, and Wettstein is a trifle too mild. Even Coenen is not quite emphatic enough. Stettin rather agrees with Guthrie, who, although having once claimed to have shown with Carrel the possibility of reversal of the circulation in the limb of a dog, deplores the fact that arteriovenous anastomosis should have been applied to the human being for circulatory disturbances of the lower extremity and prophesies its failure; for he, Stettin, believes that it is very questionable if the operation is ever justified. He believes that this procedure should be entirely eliminated from our surgical repertoire.

THERAPEUTICS

UNDER THE CHARGE OF

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The Effect of Lumbar Puncture in Delirium Tremens.—STEINEBACH (*Deutsch. med. Wchnschr.*, 1915, xli, 360) says that the cerebral pressure is increased absolutely in most cases of delirium tremens and probably is relatively increased in all. He found the cerebrospinal fluid under considerable pressure in one patient who showed inactive pupils to light—and the delirium subsided immediately after a lumbar puncture. He says that Schott-Müller has claimed that in acute alcoholic intoxication the cerebrospinal fluid is always under increased pressure and that alcohol is present in the fluid. Acting upon these observations Steinebach has systematically applied lumbar puncture for the treatment of delirium tremens. His results have confirmed his impression that the abnormally high pressure is responsible for the symptoms of delirium. He does not believe that the alcohol content of the spinal fluid is directly responsible for the delirium but is inclined to attribute the symptoms to a combination of high cerebral pressure, with a secondary poison generated by the alcoholic intoxication. The relief of symptoms following lumbar puncture is due not only to a regulation of the pressure but also to the renewal of a certain amount of poison accumulated in the cerebrospinal fluid under tension.

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lasted several days, the temperature frequently fell by crisis with corresponding improvement in the remaining symptoms. They warn against its use in the event of a complicating pneumonia, intestinal hemorrhage, a weakened cardiac action, or in cases in which the temperature is at an abnormally high level.

The Treatment of Typhoid with Autogenous Living Vaccine.—BOURKE, EVANS and ROWLAND (*Brit. Med. Jour.*, 1915, 2831, 584) after treating cases of typhoid fever with the ordinary vaccine and obtaining excellent results were led to try the effect of autogenous living vaccine as a therapeutic measure in typhoid fever. Their cases have demonstrated that this method of injecting living bacilli in suitable doses is perfectly safe. The vaccine was injected subcutaneously, as a rule in the pectoral region and was followed by a very slight local reaction, but a marked general reaction. The injection, as a rule, was followed by a sharp rise in temperature within the first few hours followed by a marked fall within twenty-four hours after the injection. Careful notes were made and in their minds there is no doubt that this treatment had a beneficial effect and tended to cut short the duration of the disease. It promotes perspiration, the aspect of the patient undoubtedly becomes brighter after injection, and the tongue becomes much cleaner. The disease was in each case diagnosed by means of blood culture. For this purpose 5 c.c. of blood were drawn from the arm and immediately transferred to 1 per cent. sodium taurocholate. From this a broth culture was prepared, and the purity and identity of the growth verified by agglutination and sugar fermentation tests. The broth culture was reinoculated into fresh broth every day and itself constituted the vaccine. No further preparation whatever was employed. The age of the culture used was generally eighteen hours, and the number of bacilli contained in it was obtained by a direct method of counting. The average number of organisms ranged from 60,000,000 to 300,000,000. They believe that their observations demonstrate that a living culture of the typhoid bacillus can be injected subcutaneously into enteric patients, not only without any deleterious effects, whatever, but, as far as the cases reported show, with decided favorable influence on the course of the disease.

The Destruction of Tetanus Germs with Ultra-violet Rays.—JACOBSTHAL and TAMM (*Münch. med. Woch.*, 1914, lxi, 2324) report that radiation of jagged wounds with ultra-violet rays will kill tetanus bacilli and the bacilli of malignant edema at the site of infection. They believe that systematic use of this method of treatment will help to prevent systemic infection. This method should not replace thorough surgical cleansing of the wound but should supplement the surgical treatment. Kromayer's lamp and the artificial high solar light may be used to generate the ultra-violet rays.

The Action of the Opium Alkaloids on the Coronary Artery and the Coronary Circulation.—MACHT (*Jour. Am. Med. Assn.*, 1915, lxiv, 1489) says that morphin, the principal opium alkaloid, produces a mild relaxation or dilatation of the coronary artery and an increase in the coronary outflow; narcotin produces the same effect in a greater

degree, and papaverin gives certainly the most marked vasodilating action of them all. On the other hand, the vasodilator effect of codein on the coronary is very slight, and that of narcein and thebain practically none at all. A most interesting phenomenon noted is the peculiar result of the synergism, or antagonism as it might better be called of morphin and narcotin. A combination of these two alkaloids instead of producing a vasodilatation, as might be expected produces practically no dilator effect at all. This antagonism apparently exists only in the dilator action of narcotin and morphin. In his experiments, Macht found that narcotin is by no means an inert drug but is quite toxic to the heart, respiration and other physiologic functions. The effect of combining morphin and narcotin seems to be rather a true synergism in which the two components play equally important parts. To a lesser extent a similar synergism has been noted between morphin and papaverin, and codein and narcotin. The commercial combinations of opium alkaloids of Straub and of Sahli were found to produce very little vasomotor change in the coronary circulation. It is hardly necessary to declare that these differences in the behavior of the different alkaloids may be of practical importance. Thus, for instance, in cases of coronary spasm, which is regarded as the commonest cause of angina pectoris, an opiate possessing a marked vasodilator action would certainly be preferable. J. Pal of Vienna, who has worked a great deal with papaverin, has actually recommended and employed that drug in angina pectoris and other conditions with vascular spasm. In choosing a suitable drug, other factors are, however, to be borne in mind. The principal other factors to be considered in the case of an opiate are its narcotic and analgesic action, its effect on the respiratory centre, and its effect on the heart. In respect to narcosis and analgesia of the six alkaloids studied, narcein and thebain fall out of consideration. These alkaloids, though derived from opium, have no sedative action. Indeed, thebain is a convulsant much like strychnin, and narcein has also an exciting rather than sedative influence on the central nervous system. Narcotin also has very little effect on pain. Of the three other alkaloids remaining, the narcotic and analgesic properties of morphin and codein are too well known to need reiteration. It is not generally known, however, that papaverin is quite an efficient drug in this respect, though attention was called to that effect by Baxt as early as 1869. In regard to action on the respiratory centre of the three drugs, morphin, codein, and papaverin, the morphin is certainly the most depressant. Macht states that papaverin is much less depressant than morphin in this respect, and codein still less so. As to the action on the heart, it may be also stated in this connection that narcotin has the most toxic action of the alkaloids studied; and morphin, though not very poisonous, is in full doses depressant to the heart. Codein and papaverin, on the other hand, were found to have no depressant action in this respect, and in small doses were found actually to stimulate cardiac activity. Inasmuch as all opium alkaloids in excessive quantities are depressant to the heart, and inasmuch as caffein is one of the chief pharmacologic antidotes to opium and is at the same time a cardiac stimulant, it was of interest to learn the action of a combination of caffein and some of the alkaloids studied. Accordingly, some experiments along these lines were made.

It was found that caffein alone dilates the coronary artery, and that this action is not antagonized by the opium alkaloids. Thus a combination of papaverin and caffein gave a dilatation of the coronary ring. In respect to the cardiac effect, it was found that caffein, given simultaneously with an opiate, produced cardiac stimulation and counteracted any cardiac depression that might otherwise have occurred Macht hopes that these observations may conduce to a more rationa therapy of cardiac conditions.

The Indications for the Subcutaneous Use of Magnesium Sulphate in Traumatic Tetanus.—USENER (*Münch. med. Woch.*, 1914, lxi, 2323) writes especially concerning the treatment of tetanus by subcutaneous injections of magnesium sulphate. He believes that it is of real value and should be used in large doses under conditions which directly threaten life—such as severe dyspnea due to tetanic spasm of the respiratory muscles, severe spasms of the esophagus, etc. The subcutaneous use of magnesium also lessens the number and severity of individual convulsions. The intradural use of magnesium should be reserved for the very urgent cases—as untoward effects, such as paralysis of respiration, are frequently seen. With regard to the strength of solution to be used for subcutaneous injection, Usener advises a solution of from 40 to 50 per cent. strength for adults in dosage of from 0.15 to 0.2 g. per kilo. In light cases a single dose may be sufficient but in severe cases and when it is necessary to secure the full effect of the drug, three or four doses at two-hour intervals should be given. In order to maintain the effect of the remedy its administration should be continued until the symptoms calling for its use have disappeared.

The Intravenous Injection of Mercurialized Serum in Syphilis.—THOMPSON (*Jour. Am. Med. Assn.*, 1915, lxiv, 1471) has devised a method of administering mercury intravenously without the unpleasant results (phlebitis and periphlebitis) which occasionally occur after the intravenous injection of mercurial salts in watery solution. He makes use of mercurialized serum and gives the details of its preparation in his article. In brief, the serum is prepared by adding an aqueous solution of mercuric chlorid to blood serum so that 7 c.c. of the mixture contains one-third grain of mercuric chlorid. Mercury albuminate which is at first precipitated on the addition of the serum is completely dissolved when an excess of serum is added; and is kept in solution indefinitely by heating the mixture in a water-bath for one-half hour at 55° C. The mercurialized serum can be kept indefinitely in sealed ampoules. Thompson gave 1.75 c.c. of the serum (equivalent to $\frac{1}{12}$ grain of mercury) as an initial dose and gradually increased this dose to 7 c.c., the equivalent of $\frac{1}{3}$ grain of mercuric chlorid. Symptoms of mercurialism developed after comparatively small amounts of mercury had been given in this way. He says in conclusion that the intravenous method of administrating mercury is not the method of choice in all cases of syphilis, but is so in certain cases, in which quick results must be brought about, and in those cases in which great pain occurs in intramuscular injections of mercury.

PEDIATRICS

UNDER THE CHARGE OF

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Ameba Colitis in a Child of Five Years.—G. J. GREIL (*Archiv. Pediatrics*, 1915, xxxii, 272) reports a case of ameba colitis in a child, aged five years. The condition began with distention and pain in the abdomen, and developed gradually into emaciation, with many blood-tinged movements a day, severe abdominal pain, and distention. On examining the stools, actively motile amebas were found. Marked improvement followed two hypodermic injections of one-tenth grain and one-eighth grain respectively during twenty-four hours. Emetin, grain one-sixth, was given every two days for three or four doses, and the child apparently recovered by rapid degrees after this. The stools were examined at the end of three weeks and again in one month, amebas were found, and the emetin given every other day for six doses. The examination at the end of this third month was negative and the patient declared cured. The case illustrates the importance of thorough and continued examination even when the patient is apparently well.

Early Pulmonary Tuberculosis in Childhood.—KENNETH FRASER (*British Jour. of Tuberculosis*, 1915, ix, 1) gives an analysis of the study of approximately 300 cases of pulmonary tuberculosis among children in elementary schools. Out of 29,750 children attending elementary schools in one county, 296 cases of pulmonary tuberculosis were diagnosed. The percentage distribution was: Whole county, 0.8 per cent. Rural: boys, 0.8 per cent.; girls, 0.7 per cent. Urban: boys, 0.8 per cent.; girls, 0.9 per cent. In point of age, the number of cases increases rapidly from 19 at five years to 37 at six years, 38 at seven years, and 40 at eight years. These figures seem to constitute a serious indictment of the influence of school life on children predisposed to tuberculosis. The returns for weight and nutrition of these cases is striking. Of this series 24 per cent. were above average weight, 10 per cent. were of average weight, and 64 per cent. were below average weight. Nutrition must be considered with weight, and at least 40 per cent. of this series showed signs of impaired nutrition, which is probably the first visible sign of tuberculosis infection. Night sweating occurred in 55 per cent. of the cases. This has no weighty significance unless the sweats are markedly heavy. Coughing occurred in 45 per cent. of cases, the dry "hacking" cough being particularly significant of incipient phthisis. In this series, in only 1 case was neither apex involved, in 76 per cent. the apices of both lungs were affected. Where one apex alone was involved the right showed three times to once in the left. Moderate dulness occurred in 40 per cent., marked dulness in 91 per cent., and very slight dulness in 23 per cent. of the cases. Friction, denoting pleurisy, and fine crepitations when localized and persistent are the most valuable auscultatory signs. Within two years, 214 reëxaminations were made and indicated that spontaneous

improvement is more common in girls than in boys, that it tends to increase from the sixth year onward, and that rural areas have a much greater tendency to develop spontaneous improvement than urban areas.

Prognosis and Treatment of Congenital Syphilis. A Plea for Notification.—LEONARD, FINDLAY, and MADGE ROBERTSON (*Glasgow Med. Jour.*, 1915, lxxxiii, 330) give a synopsis of results obtained with different methods during the last two years. The following methods were tested. Cases treated with mercurial inunction and in breast-fed children the administration of pot. iod. and hyd. perchlor. to the mother. This method uniformly shows a high death rate from the reports of other investigators and the authors' figures in 18 cases show a mortality of 66 per cent., and of 71 per cent. for children under three months. Cases treated with joha and neosalvarsan by intramuscular injections and mercurial inunction showed fairly good results but the method was discarded on account of the great pain, the necrosis, and sloughing which often occurred. Cases treated with neosalvarsan by intravenous injections and mercurial inunction; in all, 43 cases were so treated. In younger children the veins of the scalp and in older children the external jugular vein was used. Concentrated solutions were used, 0.05 to 0.3 gram to 3 or 5 c.c. normal saline. Twenty-two of the cases were under three months and including all cases that died within a year of the last injection showed a mortality rate of 45 per cent. Antenatal treatment in 7 cases is reported. This is the treatment of pregnant women by neosalvarsan intravenously and by mercurial inunction. The result was good, the children at birth and at subsequent examinations showing no clinical signs of syphilis and having negative Wassermann tests. In no case was the course of pregnancy interrupted. The uterine localization of the disease accounts for the absence of clinical manifestations in mothers of syphilitic children. Congenital syphilis, even when vigorously treated shortly after birth is difficult to cure and has a high mortality. Of all the methods antenatal treatment with salvarsan would seem to give the best results from the above series and from the reports of Sauvage with 93 per cent. of cures and Bourret and Fabre with 100 per cent. of cures. For its proper execution, however, notification in some form or other is advisable and even essential, and syphilis should be added to this list of notifiable diseases so that the great number of cases be reduced by the proper treatment.

OBSTETRICS

UNDER THE CHARGE OF

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Indications and Contra-indications for the Use of Pituitary Preparations in Obstetric Practice.—VOGT (*Ztschr. f. Geburtsh. u. Gynäk.*, 1915, Band lxxvi, Heft 3) contributes an interesting paper based

upon his observations in Kehrer's clinic in Dresden. He has been accustomed to use this drug at the end of the period of dilatation and during the stage of expulsion, especially when delay occurred through inefficient uterine contractions; also in the case of primiparas much above the average age for child-bearing, in deficient development of the uterus, in constitutional conditions depressing the patient, and in premature rupture of the membranes with escape of amniotic liquid, pituitary extract had given good results. In moderately contracted pelves where disproportion is not great, the writer obtained good results by giving pituitary extract. In contracted pelvis, however, the field for the use of pituitary extract is a very limited one. When the patient has had pains for some time, which grow weak, the disproportion between mother and child being a very moderate one, pituitary extract may be given to increase the power of uterine contractions. Care must be taken that the pelvis is not highly contracted, or the child excessively large, but in moderate degrees of contraction the Mercurio-Walcher position will be found especially valuable. Three illustrated cases are reported in which the use of pituitary extract seemed valuable. In cases where fever develops during labor, the use of pituitary extract brought about spontaneous delivery and spared the patient the dangers of operative interference in these cases. The writer has also had good results in giving pituitary extract when he was using dilating bags to expedite labor. The dread of operative interference is so strong in some that it is difficult to obtain permission to perform operations. In breech presentation where every effort is made to secure spontaneous expulsion, pituitary extracts may also be of considerable value. Those operations whose function it is to increase the size of the pelvis, such as hebostiotomy and subcutaneous symphysiotomy, will give better results if the use of pituitary extract be combined with the operation. The writer has little of personal experience to give in the use of pituitary extract in placenta previa. After Cesarean section this substance is useful, especially in cases where compression of the uterus has been made by a broad bandage during the time of actual delivery. The drug is useful and, when the placenta has been retained, the dangerous procedure of removing it by the hand may sometimes be avoided by giving pituitary extract, when the uterus will expel its contents spontaneously. In estimating the contra-indications for the use of the substance, he was unable to find evidence that pituitary extract entered the blood of the child when given to the mother during labor. It was possible, however, to bring on pains in this manner, so vigorous as to subject the child to unusual pressure, with its unfortunate result. As regards the mother, the drug should not be used when the condition of the kidneys is bad, as it is sometimes injurious and increases blood-pressure in such cases. It is interesting to observe that in a case of albuminuria with severe nephritis, and with a blood-pressure of 180, pituitary extract was given just after the child had been delivered by embryotomy. The drug seemed to have very little effect. In cases of cardiac disease, where the heart muscle is inefficient in maintaining circulation pituitary extract is not contra-indicated, but often acts as a stimulant, as do camphor, digitalis, and caffein. The strongest contra-indication is found in symptoms of threatened uterine rupture. The presence of the contraction ring

should act as a warning against the use of the drug. Injurious complications arising from relief by pituitary extract must be rarely observed, as very few have been reported. The dangers in the use of the drug are few in proportion as it is correctly and carefully employed. It has no cumulative influence, and can be used at intervals of one or two hours at all stages of labor. The unpleasant symptoms sometimes seen, slowing of the pulse, threatened collapse, paleness, syncope, dilated pupils, sweating, and general depression, are peculiar to the individual patient. Occasionally very violent uterine contractions occur which are attended with considerable pain. Spasmodic contraction of the internal portion of the cervix and tetanus of the uterus have also been observed. In using these preparations the heart sounds must be watched by auscultation, when it will be noted that the fetal heart beat is often slower than normal. Thus the fetal heart has beat as slowly as 40 to the minute in occasionally observed cases. So the discharge of meconium is also a sign of dangerous pressure. Should the fetal heart be much disturbed the drug must be stopped, and prompt delivery effected by some operation. The writer has investigated a number of cases where death occurred in the child shortly after labor, or during labor, but had never found a case where the drug could be justly considered the sole cause of the accident. In mentioning the different preparations which he employed, five are enumerated: one an American preparation, one English, one French, and two German. The latter had been used in 7600 labors.

Changes in the Maternal Decidua Producing Complications During Pregnancy.—HINSELMANN (*Ztschr. f. Geburtsh. u. Gynäk.*, 1915, Band lxxvi, Heft 3) has studied microscopically the parietal decidua in pregnancy when abnormalities in the chorion were present. He finds that violent impaction by the fetus is responsible for some of these conditions which has produced changes in the cells of some of the parts. Unquestionably, the amniotic liquid and also bacteria, have some influence. Necrosis is present in the deep layers of cells, or where there are channels through the decidual nuclei, the influence of the amniotic liquid can be excluded; so also, can possibly that of bacteria. In some of these cases hydrorrhea develops, and in others areas in the chorion become necrotic, and complications on the side of the fetus may develop.

GYNECOLOGY

UNDER THE CHARGE OF

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Acute Traumatic Displacement of the Uterus.—The ability of a single, acute trauma to cause displacement of a previously normal uterus has often been called into question, and not a few gynecologists are inclined to doubt the possibility of such an occurrence. In a paper

recently presented before the New York Academy of Medicine, however, BARRINGER (*Am. Jour. Obst.*, 1915, lxxi, 758) reports six cases in which she believes this type of displacement to have occurred. The ages of these patients ranged from fifteen to forty-three years; all but one were nulliparæ at the time of the accident. In two cases the accident consisted in a fall on the back or side in the supine position, incident to being hurled from a car; in two others there was a sudden fall in the sitting position on the ice or a hard floor; in one the history was of a sudden unexpected strain in lifting, while in the sixth case the exact nature of the accident could not be determined, as the patient lost consciousness at the time. All the women were confined to their homes for periods varying from a week to several months. The symptoms that have been most prominent in the author's experience in cases of this type may be divided into four groups, as follows: (1) Pain, usually in the lower portion of the back, over the sacrum and coccyx, sometimes in the region of the rectum, with painful defecation; (2) Bladder irritability, this being expressed by great urgency and frequency of micturition. It may be so severe as to dominate the clinical picture. (3) Change in type of menstruation. In one of the patients a uterine hemorrhage occurred immediately following the accident; in two, menstruation became painful, prolonged, and too frequent; one case had not menstruated since the accident up to time of examination, and one showed no change. (4) Characteristic posture and gait. The shoulders are generally stooped forward, with head carried slightly forward, the dorsal and lumbar spine held in a position of slight kyphosis, the whole appearance suggesting the posture of traumatic lumbago. The lower abdominal muscles may be more or more contracted, the patient supporting them with her hand; the gait is slow and guarded. On vaginal examination, the author usually found one of three conditions: either (1) the uterus had swung over 180° on its pivotal point in the pelvis. The fundus lying in third degree retroversion, with the cervix in its normal place; (2) there was a moderate degree of prolapse; or (3) the uterus was a whole had been driven back into the hollow of the sacrum in varying degress of retroversion, fundus and cervix being incarcerated there. Treatment of course consists in reduction as soon after the accident as possible. In one instance, in which the diagnosis was made a day or two after the accident the uterus snapped back into place; the young girl was kept on her abdomen for a week, and was warned to keep the bladder emptied frequently. She made a complete recovery, has since married, and has had no difficulty with retroversion of the pregnant uterus. In another case, in which a couple fo weeks had elapsed since the accident, congestion made the reduction more difficult, necessitating tamponing the posterior fornix, and the employment of hot douches. Recovery here, also, was complete and permanent, the patient having been followed for over five years. In a third cases the condition was discovered only after two months of great discomfort; here treatment by means of a pessary was necessary for weeks, and the uterus never returned to as perfect position as the others. The author emphasizes the importance of early diagnosis in these cases, since if the conditions remains unrecognized, the patient will probably drift into years of invalidism, from which she might have been saved.

Treatment of Chronic Ulcer of the Vulva by Salvarsan.—FISICHELLA (*Policlinico*, 1915, xxii, 485) says that he has observed in the past five years twenty cases of chronic, indolent ulcers of the vulva, in all of which the Wassermann was positive. He has come to consider syphilitic infection of great importance in the etiology of this local condition although in the one case in which he attempted to demonstrate spirochetes in smears from the ulcer, he was unsuccessful, probably owing to the fact that the patient had been subjected to vigorous local and systemic treatment. Clinicians, he says, have generally refused to consider vulvar lesions of this type syphilitic in origin, even when occurring in obviously syphilitic subjects, owing to the failure of the ordinary specific treatment with mercury and the iodides to effect a cure. Fisichella considers, however, that these lesions are in fact comparable to many others—such as some gummas occurring in bones and on mucous surfaces, certain cutaneous keratoses, etc.—which, while extremely rebellious to mercury and iodides, yield quickly to small doses of salvarsan. In support of this idea, he cites the cases of three prostitutes who came into his ward for treatment. In all of these women the Wassermann reaction was positive, and plain clinical evidences of syphilis were present. In addition to other lesions, all had indolent, phagodenic ulcers of the vulva of long standing. Active treatment by means of mercurial inunctions, biniodide, and KI, together with local antiseptic applications, had been without effect, but the changes produced after small doses of neosalvarsan were little less than marvelous. The drug was given by the usual intravenous method, starting with 0.15 gm., a second dose of 0.30 gm. being given four days after the first, and a third of 0.40 gm. five days after the second. Immediately after the first administration, improvement began to be noticed; healthy granulations were formed, and gradually cicatrization began from the edges, complete healing taking place in all three cases within fifteen days, notwithstanding the fact that these ulcers had resisted all other methods of treatment for years. Subsequent examinations of the patients have shown the result to be permanent, nothing remaining at the site of the original ulcer but a smooth, firm cicatrix, with a slightly pigmented border.

OPHTHALMOLOGY

UNDER THE CHARGE OF

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Elliott's Operation in Glaucoma.—LUNDSGAARD (*Klin. Monatsbl. f. Augenhk.*, February and March, 1915, p. 209) concludes from his experience with this operation that the procedure is a very valuable addition to

the therapy of glaucoma, in suitable cases relatively certain in its results, and of facile execution. Three years additional experience with it, however, has convinced the author that this operation entails greater risk than he was first inclined to believe. He, therefore, does not now favor operating in every case of increased tension and would not, like Elliott, operate as a prophylactic measure. Where the tension is relatively low, 30 to 35 mm. without loss of field, miotics have given satisfactory results; where the tension is higher than 30 mm., especially if miotics are without effect, the writer operates in all cases of simple glaucoma, even where the fields have been markedly affected and the visual acuity lowered.

In secondary glaucoma (uveitis with increased tension) the reporter would be very conservative as regards operating. To avoid secondary perforation and infection he recommends making the conjunctival flap as thick as possible and he considers the iridectomy to be, to a certain extent, a preventive measure, in that it prevents secondary prolapse of iris, which event he believes favors perforation, for which reason the prolapse is to be excised whenever it occurs.

The Effects of Various Kinds of Rays upon the Crystalline Lens.—Chalupecky (*Wien. med. Wchnschr.*, 1914, pp. 27, 270) has attempted by suitable experiments to gain an insight into the mechanism of the occurrence of opacities of the crystalline lens, following the action of powerful sources of electricity as well as the influences of various kinds of rays. By means of chemical analyses and experiments upon guinea-pigs, he was enabled to confirm Widmark's views as to the direct influence of the ultra-violet rays upon the lens. On the other hand, he was unable to show by his experiments with the Roentgen rays, even with intense radiation, any chemical changes in the structure of the crystalline. A like negative result occurred in his experiments with radium chloride, with Roentgen rays and with mesothorium.

Glaucoma and Blood-pressure.—MacRae (*Ophthalmoscope*, April, 1915, p. 168) examined 20 cases of primary glaucoma and a number of control cases with a view to determining the influence of the blood-pressure in glaucoma. His results are not uniformly either in favor of, or against, the theory that the average blood-pressure in glaucoma is high, though they tend to oppose that view. That the blood-pressure helps to maintain the eye tension, no one will deny, but the latter may be affected in many ways which have no connection with, and no effect on, blood-pressure; and conversely the blood-pressure may alter greatly without any corresponding observable effect upon the intra-ocular tension. That blood-pressure is of any importance at all in the causation of glaucoma is very doubtful. (It may be recalled that Dunn and Jackson have invariably found the blood-pressure above normal in primary glaucoma.)

Glaucoma in the Young.—From an exhaustive study of the clinical material of the University Eye Clinic of Tubingen, Haag (*Klin. Monatsbl. f. Augenhk.*, February and March, 1915, p. 133) comes to the following conclusions: General diseased conditions, particularly dis-

individual of good growth power whose normal growth processes are not being used shows rapid growth of neoplasms. Infections take the weak; cancer takes the strong mice. Reduction of food increases infectability, lowers the cancer rate. Vigorous growth increases the cancer rate, lowers infection rate. Slight infection kills a frequent female, but tumor growth is slackened by frequency. Cancers occur only in cancer strain; infections occur in any strain. Infections spread in one or to other cages; cancer does not spread in the same cage nor to other cages by contact. Mice feeding on dead infected mice may become infected, but mice do not contract cancer by feeding on dead cancerous mice. Control mice fed on cancer material do not contract cancer. Cancer is a disease of middle and advanced age when normal growth processes are confined to regeneration and reproduction; infections are diseases of early life when growth processes are largely accretions in quantity and in complexity. Cancer differs from infection, since it follows the laws of heredity, and since it can be bred into or out of strain at will. Since cancer is transmitted, rather as a tendency to occur from a given provocation, an over-irritation, the elimination of over-irritation in one of cancer ancestry should materially lower the rate, and the eugenic control of mating so that cancer shall not be potential in both should also very materially decrease the incidence of human cancer.

The Prevention of Typhus Fever.—ANDERSON (*Public Health Reports*, April 30, 1915, p. 1303) discusses the recent work on typhus fever and the methods of its prevention and control based on these researches. He states that there is no experimental evidence to support the view that typhus is acquired in any manner other than by the intermediary of lice which have previously fed on persons sick with typhus. From this fact it is possible to deduce the fundamental procedures on which the control of the disease may be based, and these procedures may be grouped under four general headings: The first is, measures for the reduction of lice infestation among the population in general. These measures are, to a large extent, educational except in institutions and places over which the sanitary authorities have supervision, such as bath-houses, lodging-houses, and similar places. In surroundings where lice may find lodgment efforts should be made for the destruction of lice and their eggs. These efforts consist in the use of insecticides, both chemical and physical, bearing in mind the important point that the louse requires frequent feedings on blood and is, therefore, most apt to be found on recently used clothing or bedding. Under the second heading should be considered measures for the eradication of all lice and their eggs found on the bodies, clothing, bedding and surroundings of cases of typhus, suspects, and contracts. The first essential under these procedures is the institution of measures requiring the prompt reporting to the sanitary authorities of all cases of suspected cases of typhus fever. These cases should be promptly seen and the inspector satisfied that the surroundings are free from lice, in which case the patient may, without danger to the community, be treated at home. If, however, such is not the case, the patient should at once be removed to the hospital and the place from which he is removed should be treated for destruction of all lice and their

eggs. All patients, suspects, and contacts should be bathed, the lice and their eggs in the hair and clothing destroyed, after which they should be given a clean change of clothing. They should then be kept under observation for twelve days. Under the third heading are measures such as should prevent or minimize the possibility of persons near cases of typhus being bitten by lice. It should be kept in mind that the radius of action of the louse is much shorter than that of the mosquito in yellow fever or the flea in plague. The transference of lice, and consequent infection with typhus, from one individual to another requires rather intimate association with lice-infested persons or their surroundings. And by reason of the fact that the louse requires frequent feedings to maintain life, this means for practical purpose surroundings recently occupied by persons and possibly by animals. Under the fourth heading it is suggested that persons desiring to enter localities in which the virulent form of typhus is prevailing in an epidemic form should be inoculated with the mild form of typhus fever so widespread in the United States, the case mortality of which is not over 1 per 100 while the case mortality of the typhus in Serbia, for example, is possibly 20 or more.

Diphtheria Bacillus Carriers.—ZINGHER and SOLETSKY (*Proc. New York Path. Soc.*, N. S., 1915, vol. xi) found that 4 to 8 per cent. of individuals in localities where diphtheria is endemic are carriers of bacilli morphologically and culturally like the diphtheria bacillus, but non-virulent in 30 to 50 per cent. of the cases. At the Willard Parker Hospital, Wilcox and Taylor found 4.5 per cent. of the cases admitted to the scarlet fever wards were bacillus carriers and of the isolated organisms only one-half were virulent. According to Neisser individuals who become persistent carriers after an attack of diphtheria show only non-virulent forms in fully 20 per cent. of cases. Such individuals could be discharged from quarantine if this fact were established. Roux and Yersin are of the opinion that both virulent and non-virulent are present in cases of diphtheria. The preponderance of each strain, however, varies with the severity of the disease, but that during convalescence all virulent strains undergo a definite diminution in virulence. Graham-Smith, Loeffler, as well as Park and Williams believe that the individual virulence or non-virulence is permanent with the strain. Dr. Williams and others have not been able to change the non-virulent into a virulent strain, as claimed by Thiele and Embleton for the Bacillus Hoffmani. It is probable that the virulent strains remain true to type and that the same applies to the non-virulent strains.

Non-virulent strains cannot be separated from the virulent by morphological or cultural characters. Hence, animal tests must be employed for this determination. M. Neisser uses a method analogous to that of Römer for the determination of small amounts of diphtheria antitoxin in sera. This consists of intracutaneous injection of varying mixtures of the unknown antitoxic serum and a standard antitoxin. A slight excess of toxin produces a local necrosing lesion, while a neutral or over-neutralized mixture shows no effect on the tissues at the site of injection. Zingher and Soletsky have improved Neisser's method by using 2 guinea pigs for the testing of from 4 to 6 different strains. One guinea pig serves as a control and receives about 200 units of antitoxin

intracardially at the time of making the test, or intraperitoneally twenty-four hours before. Both pigs are injected with suspensions of the cultures to be tested intracutaneously. A fresh twenty-four-hour growth from an ordinary Loeffler slant is suspended in 25 to 30 c.c. of normal salt solution; 0.1 c.c. is injected into the skin. The results of the tests are noted in twenty-four to forty-eight hours. Virulent strains produce a definite local inflammatory lesion, which shows a superficial necrosis in forty-eight to seventy-two hours. In the control pig, the skin remains normal. With non-virulent strains no lesions will be found in either control or test animal.

PATHOLOGY AND BACTERIOLOGY

UNDER THE CHARGE OF

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Arterial Degeneration.—F. W. ANDREWES (*Annual Report of Local Government Board*, 1913–14, Appendix B, p. 151) has been appointed to carry on a series of investigations on the nature and cause of arterial degenerations. The present is the second of his reports and is divided into two parts. The first line of investigation concerned the degree to which infectious conditions played a part in the premature occurrence of arterial disease. The second part of the investigation was to find some criterion by which the degree of degeneration could approximately be judged. Some very interesting findings are reported concerning the infective process of the arterial wall. The author not only studied the histopathology of the arteries but a bacteriological analysis was undertaken of the tissues of the larger arteries. By his technique he was able to obtain cultures of the arterial tissues quite apart from the presence of bacteria within the lumen. Out of six cases of Streptococcus septicemia the organism was isolated four times from the aortic wall, the staphylococcus was obtained twice out of three cases of septicemia, while in seven cases of malignant endocarditis the organism was not found in the arterial tissues. Similar negative findings were obtained in pneumonia. On the other hand, a positive result was once obtained out of five cases of acute rheumatic fever. Associated with B. coli infection the aorta was invaded by this organism in four out of five cases. These findings are important in the light of recent work demonstrating the presence of an inflammatory reaction in the arterial

wall in many cases of infectious disease. Andrewes found that inflammatory reactions were present in Staphylococcus and Streptococcus septicemia, malignant endocarditis, scarlet fever, acute rheumatic fever, measles, B. coli infection, and syphilis. He points out that insofar as the destructive nature of the disease is concerned, syphilis stands by itself. The study, in general, confirms and amplifies those previously made by others. As every individual suffers not a few infective processes during his lifetime, each of which probably has some effect upon the vessel wall, the author believes it very suggestive that we here are dealing with the cause of premature arterial degeneration. In the subsequent investigation of finding an index of the grade of degeneration it was shown that the calcium content of the arteries is a useful criterion. The method, however, is too cumbersome to serve any other than a suggestive study. He found that the calcium content remained low and fairly uniform up to the twentieth year. From this until the thirty-fifth year there was a gradual increase, while after middle life, the calcium content rises markedly. Furthermore, it was found that the calcium contant of the arteries in disease was greatly increased and he believed that the relative amount is a good index of the degree of degeneration. For syphilis, however, these figures have not the same value, as the calcium content is not equally increased when syphilis alone is present, but varies with the association of it with a true sclerosis of the artery.

Cancer of the Thyroid in Graves' Disease.—Although we associate Graves' disease with certain structural changes of thyroid gland, not a few cases are on record in which the characteristic hyperplasia was wanting and an entirely different process present in the gland. Langhans classified the epithelial changes of the thyroid in seven groups, each of which has been described associated with Graves' disease. Lyon (*Ztschr. f. Krebsforsch.*, 1914, xiv, 501) described a case of columnar cell cancer of the thyroid in a female, aged twenty-one years. She had typical symptoms of Graves' disease with enlargement of the right lobe. The tumor was removed as well as a number of cervical lymph glands which were involved in metastatic growth. The primary tumor as well as the secondaries contained more or less colloid. The growth was typically cancerous and infiltrated the gland capsule and surrounding tissues. The cancerous alveoli showed no papillomatous ingrowths as is usually seen in hyperplasia of the thyroid. The author believes that the new growth developed upon a primary hyperplastic goitre or that cancer and Graves' disease simultaneously developed in a colloid struma. Whether the colloid material produced in cancer of the thyroid is abnormal and assists in producing symptoms he was unable to say.

Tumors in Amphibia.—Recent studies on tumors have shown that they are widely distributed in all types of animals and particularly in vertebrates. Spontaneous tumors of rats, mice, fowl and fish are now well known to us. A number of investigators have described tumors in amphibia. The majority of these were located in the skin and were of the nature of fibroma, adenoma, and cancer. The first of these were described by Eberth, 1868, consisting of multiple adenomata of the

skin of a frog. The character of the tumor in these animals is not easy to determine and some discussion respecting the origin of the tumor cells has arisen. It is suggested that the masses are associated with the presence of distoma and neomatodes which are so commonly present in the skin glands. Hypernephroma and tumors of the ovary have also been described. PENTIMALLI (*Ztschr. f. Krebsforsch.*, 1914, xiv, 623) observed multiple tumors beneath the skin of a frog which he was unable to transplant to new animals. Some of these tumors had ulcerated through the skin but not all were adherent to it. The small tumor masses were situated in the superficial portion of the corium. He believed that each of the multiple tumors was primary and not of metastatic origin. The tumor was of adenomatous type with some character of malignancy. They apparently began in the glands of the skin.

A Cytological Study of the Exudate in a Case of Tuberculous Pleurisy. —KIPP (*Folia Hematologica*, 1914, xviii, 43) studied the cells of a tuberculous exudate at intervals and observed the change in the relative counts from the acute process to the stage of healing. At the beginning an endothelial type of cell was found in greatest abundance. These, however, were not all of the same kind, some being true endothelial cells, others myeloblasts and some lymphoblasts. Subsequently the cell count changed and the proportion of lymphocytes increased considerably. Finally, at the end of three weeks the endothelial type of cell had almost disappeared while the eosinophiles and lymphocytes were the most prominent type present. The change in the cell count followed the clinical course from an acute to a chronic stage of the disease. He believes that the cytological study offers a means for prognosis. He furthermore points out that the cell picture of the tuberculous exudate is not a constant one and that a high lymphocytic count is not always present. The previous findings of others are extensively discussed in the text. The exact meaning of the increase of eosinophiles in tuberculous exudates is not well understood and is difficult of comparison in acute infections where their presence is so frequent in the late chronic stages. On the other hand, however, eosinophiles appear during the acute stages of some cases of sepsis, lues, cysticercus, influenza, and typhus. It is suggested that the eosinophiles in late tuberculous lesions appear as a local response and are associated with the myelocytes and certain forms of endothelial cells.

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